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BIOMEDICAL ENGINEERING AND INSTRUMENTATION BRANCH

DIVISION OF RESEARCH SERVICES

NATIONAL INSTITUTES OF HEALTH (U.S.)

ANNUAL REPORT FY 1989

Dr. Murray Eden, Chief

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1989

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DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10001-21 BEI

PERIOD COVERED
October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Pharmacokinetics

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

R.L. Dedrick	Chief,CHES	BEIB, DRS
Others:		
C. Sung	Staff Fellow	BEIB, DRS
F.Farris	Southeastern Coll. of Pharm. Sci.	
F.King	North Carolina A&T Univ.	
R.J. Lutz	Chemical Engineer	BEIB, DRS
P.F. Morrison	Physical Scientist	BEIB, DRS

COOPERATING UNITS *(if any)*
CPB-NCI, DR-CC, NTP-NIEHS, SNB-NINCDS, NHLBI, NMOB-NCI and PB-NCI

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Chemical Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.7	1.5	0.2

CHECK APPROPRIATE BOX(ES)
☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Pharmacokinetic models are developed for the distribution and disposition of drugs, environmental contaminants, and endogenous metabolites in animals and humans. They provide a plausible set of equations that can be used to extrapolate data from animals to humans and thereby improve chemotherapy and risk assessment. Consideration of regional drug delivery has continued with emphasis on intra-arterial and intracavitary administration. Drug streaming from arterial catheters appears to be a frequent problem leading to nonuniform distribution of drug in the infused tissue and compromising studies of toxicity and therapeutic effect. Work is in progress on the development of a physiological pharmacokinetic model for methyl mercury and inorganic mercury in the rat. Work is also in progress on the adaptation of a pharmacokinetic model for cis-diamminedichloroplatinum(II) to other platinum-containing complexes. Increased emphasis has been placed on the pharmacokinetics of macromolecules such as monoclonal antibodies and immunotoxins.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10034-12 BEI

PERIOD COVERED
October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Three-Dimensional Histological Reconstruction

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

S.B. Leighton	Mechanical Engineer	BEIB, DRS
A.M. Kuzirian	Neuroanatomist	LB, NINCDS

COOPERATING UNITS *(if any)*
LB, NINCDS

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Mechanical Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.2	0.2	0

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A semi-automatic system for acquiring three-dimensional structural information about histological material is being developed. The system should be faster and more reliable than techniques that use serial sections, although resolution may be limited. In brief, an embedded tissue block will be fixed relative to a scanning electron microscope imaging system, the surface of the block will be imaged and the image stored, and successive slices will be removed by a built-in microtome. Handling and registration of thin sections will thus be eliminated. Human and computer pattern recognition will transform the resulting set of images into a three-dimensional reconstruction. Oxygen plasma etching has been found to give sufficient topographic relief that the resolution of the images is now limited by the SEM and not by the preparation technique. The images of Hermissenda Crassicornis obtained by this technique correlate well with TEM images of the same tissue.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10039-12 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Biophysical Instrumentation and Methodology

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

Marc S. Lewis	Research Chemist	BEIB, DRS
Allen P. Minton	Research Chemist	LBP, NIDDK
Dan L. Sackett	Senior Staff Fellow	CB, NIDDK

COOPERATING UNITS *(if any)*

LBP/NIDDK

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Microanalysis

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.4	0.4	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The project is designed to develop new instrumentation and methods and to improve existing instrumentation and techniques for the characterization of biological macromolecules and for study of their interactions. Analytical ultracentrifugation, the techniques ancillary to it, and methods of data analysis using mathematical modeling appropriate for these techniques are the major areas of interest.

Studies on the application of mathematical modeling to problems of ultracentrifugal analysis have continued. The applications of these studies are described in the project report 10184-06. Major progress has been made in the development of data acquisition systems. Two new data acquisition systems for the analytical ultracentrifuge have been developed. The Macintosh II analog-to-digital acquisition system has also been completed and a direct digital acquisition system using the Macintosh is nearly completed. New methods of performing experiments and analyzing data have been developed and work is continuing in this area.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10043-12 BEI

PERIOD COVERED
October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Fiber Optic Probes

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

John I. Peterson	Chemist	BEIB, DRS
Einar Stefansson	Asst. Prof.	Dept. Ophthal., Duke University Medical Center

COOPERATING UNITS *(if any)*
RVR and EICB

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Chemical Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.8	.8	

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A suitable device is needed for the direct measurement of oxygen partial pressure (PO_2) in blood and tissue for both clinical and research applications. Methods currently available for measuring PO_2 lack convenience, reliability, speed, and applicability to many situations of interest. Efforts to develop electrical sensors have not been successful. It is desirable to have a very small PO_2 sensor that can be inserted into a blood vessel or tissue with little disturbance, which will provide instantaneous PO_2 monitoring for either short or extended periods of time. A fiber-optic sensor is ideal for this application, with the advantage, for physiological use, of very small size and flexibility, safety, and low cost. A PO_2 sensor has been developed, based upon the principle of fluorescence quenching by oxygen. The feasibility of the sensor and its satisfactory performance have been demonstrated in *in vitro* and *in vivo* tests in preceding years. The development of the sensor in the form of a needle probe was done, and an instrument suitable for research applications was developed.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS-10097-09 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Studies in Cardiovascular Dynamics

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

R.S. Chadwick	Head, Theor. Biomech.Group	BEIB, DRS
J. Ohayon	Lecturer	U. of Paris
M. Lewkowicz	Visiting Fellow	BEIB, DRS
C. Oddou	Professor	U. of Paris
A. Azencot	Senior Researcher	INSERM U. 120
B. Levy	Director	INSERM U. 141
A. Al Droubi	Staff Fellow	BEIB, DRS
I. Liang	Staff Fellow	Surgery, NHLBI

COOPERATING UNITS *(if any)*

INSERM U.120 U.141, University of Paris XII, Laboratory of Physical Mechanics, Surgery Branch, NHLBI

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Mechanical Engineering Section

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
2.3	2.3	

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

We have refined our existing model for myocardial and ventricular mechanics to include the effects of collagen on the elasticity of the myocardium and filling of the left ventricle, wall thickness and curvature effects, pathological fiber organization, myocardial blood flow, myocardial oxygen demand, effects of electrical activation patterns, interaction with right ventricle, and dynamic vibrations. The model was used in conjunction with ultrasonic kinematic data, gated radionuclide ventriculography, and left heart catheterization data, and implanted ultrasonic crystals to determine performance parameters. The physiological relationships between phasic coronary arterial, venous, and left ventricular pressure and blood flow were determined during a long diastole and control conditions A theoretical model was developed to describe contraction of arterioles, and will be used to study mechanisms of hypertension. Theoretical models investigating residual stress in the myocardium and contraction with an ischemic zone are being developed.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10098-09 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Laser Instrumentation for Vitreous & Cardiovascular Microsurgery

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

R.F. Bonner	Physicist	BEIB, DRS
P.D. Smith	Physicist	BEIB, DRS
M. Leon	Sr. Investigator	CB, NHLBI
A. Bartorelli	Fellow	CB, NHLBI
Y. Almagor	Fellow	CB, NHLBI
R. Neville	Guest Fellow	CB, NHLBI
C. Kupfer	Director	NEI

COOPERATING UNITS *(if any)*

Clinical Branch, NEI; Optical Science Branch, Naval Research Lab; Cardiology Branch and Surgery Branch, NHLBI; Quantronix Corp.; Infrared Fiber Systems; MCM Labs; Intratherapy, Inc

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Electrical and Electronic Engineering

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
2.5	2.5	

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This program covers the long-standing development of laser microsurgical techniques that initially centered on ophthalmological applications and systems of interest in that field (pulsed carbon dioxide lasers and pulsed ND:YAG slit lamp-based laser systems). Its primary focus for the last 3 years has been in cardiological application of lasers, in particular laser angioplasty. In order to develop new laser microsurgical techniques in this new field, it was necessary to analyze a variety of laser sources and their tissue effects and the feasibility of transmission through flexible fiber optics. Excimer lasers coupled to fused silica fibers were examined, as well as more conventional sources (pulsed carbon dioxide and Nd:YAG lasers and continuous-wave argon and dye lasers). New IR laser sources have been developed (in conjunction with Naval Research Lab and Quantronix Corp.) which utilize strong water absorption and can be transmitted through low-loss, cladded optical fibers. They include the first use of the Erbium:YAG laser @2.94um through zirconium fluoride optical fibers and the Thulium:YAG (Cr-doped) @ 1.96-2.01um through low-OH silica optical fibers.

Our collaborations with the NRL and various industry groups have led to a variety of prototype laser microsurgical systems for angioplasty studies. The collaboration with MCM Labs has led to clinical trials of peripheral and, more recently, coronary laser angioplasty using a pulsed dye laser with computer-controlled fluorescence guidance. Application of our infrared lasers (particularly the Tm:YAG and silica optical fibers) to laser angioplasty systems is proceeding with parallel development of a clinical infrared version of the fluorescence guidance system and a new intravascular ultrasound/laser catheter.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10109-09 BEI

PERIOD COVERED
October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Adjunctive Heat Treatment of Cancer

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

R.L. Levin	Biomedical Engineer	BEIB, DRS
J. Delannoy	Fogarty Fellow	ROB, NCI
C. Charny	NRC Fellow	BEIB, DRS
D. LeBihan	Fogarty Scientist	DR, CC
D. Hoult	Physical Scientist	BEIB, DRS
R. Turner	Fogarty Scientist	BEIB, DRS
C-N Chen	Physical Scientist	BEIB, DRS
E.J. Glatstein	Chief	ROB, NCI

COOPERATING UNITS *(if any)*
Radiation Oncology Branch, NCI; Diagnostic Radiology, CC

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Mechanical Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
3.5	3.5	0.5

CHECK APPROPRIATE BOX(ES)
☒ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of this project is to develop adjunctive hyperthermia modalities for cancer treatment through theoretical and experimental studies of the spatial and temporal variation in the temperature field of tissues subjected to radio-frequency electromagnetic radiation. Currently, we are (1) measuring the patterns of energy deposition produced by a mini-annular phased array (MAPA) applicator within various types of extremity phantoms; (2) describing the electromagnetic fields of a MAPA in terms of its design parameters; (3) describing the transient thermal profiles within limbs produced by a MAPA; and (4) describing the systemic temperature and cardiac changes associated with heating various regions of the body. We are also developing a non-invasive method for measuring temperature using magnetic resonance imaging. These studies are forming the basis for the clinical system currently being tested under the auspices of a recently approved Phase I clinical protocol.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10112-09 BEI

PERIOD COVERED
October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Analysis of Microcirculatory Blood Flow by Laser Doppler Scattering

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

R.F. Bonner	Physicist	BEIB, DRS
T.R. Clem	Electrical Engineer	BEIB, DRS
H. Wagner	Section Chief	LNNS, NINCDS
T. Delaney	Sr. Investigator	ROB, NCI
R. Nossal	Sr. Res. Physicist	PSL, DCRT

COOPERATING UNITS *(if any)*
HB, NHLBI; CB NEI; LCI, NIAID; ROB, NCI; SN, NINCDS; LAP, DCRT; MedPacific,Inc, Seattle,WA; TSI, Inc, St. Paul,MI; Neurology and Gastroenterology Depts., USUHS, Bethesda, MD

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Electrical and Electronic Engineering

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.4	0.4	

CHECK APPROPRIATE BOX(ES)
☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
 ☐ (a1) Minors
 ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project has developed a clinically-useful method (laser Doppler instrument and its theory of operation) for clinical measurements of microcirculatory blood flow, the density of flowing red blood cells (RBCs), and mean RBC velocity. Assistance has been given to the commercialization of this methodology and its application to clinical research. Our clinical studies have been directed toward examining normal and abnormal microvascular dynamics through noninvasive clinical studies of skin and nasal mucosa, and in intra-operative clinical studies of muscle and CNS. Collaboration with USUHS is directed toward developing endoscopic application of this technology. Considerable theoretical work has been directed toward an adequate construct with which to interpret the physical measurements and refining the accuracy of the microcirculatory measurements. We have discovered abnormal microcirculatory patterns and responses in the skin of patients with sickle cell disease, hypertension, certain cardiac circulatory syndromes, diabetes, and skin cancer. The microcirculatory effects of therapy are monitored with this technique, affording a better understanding of the microcirculatory component of these diseases.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10122-08 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Microcomputer Applications for the NIH Bio-Technology Unit (Pilot Plant)

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

T.R. Clem, Sr.	Electronics Engineer, EEES	BEIB, DRS
Other Investigators:		
Y. Shiloach	Chief, Bio-Technology Unit	LCDB, NIDDK

COOPERATING UNITS *(if any)*

LCDB - NIDDK

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Electrical and Electronic Engineering Section

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.0	0.75	0.25

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The NIH Bio-Technology Unit (Pilot Plant) has various instrumentation needs that have not been previously addressed and is using some cumbersome techniques and/or outdated equipment. This project has been concerned with satisfying these instrumentation needs using modern equipment and low-cost desktop size personal computers (PCs). Several PCs have been acquired and have been installed to supply a variety of services, including process control, data acquisition, data analysis, and administrative functions. The instrumentation and process control functions use commercial equipment, as much as possible, and are interfaced using standard I/O connections, such as the IEEE-488 GPIB and the RS-232 Serial I/O ports as well as using direct digital and analog I/O components in the desktop computer.

Using these techniques allows changes in the parameters measured or controlled to be accomplished relatively quickly and easily. Utilizing the computational capabilities of the computer/controller allows initial selection of the operating parameters and dynamic alteration of these parameters as the process continues, thus allowing optimization of yields or detailed study of the process parameters.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10146-07 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Prosthetic Urethral Sphincter

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

S. B. Leighton	Mechanical Engineer	BEIB, DRS
Steven Scoog, M.D	Staff Physician	WRAMC
T. Radebaugh	Senior Staff	BRCM, NIA

COOPERATING UNITS *(if any)*

BRCM, NIA and DCT, NCI

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Mechanical Engineering Section

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.15	.15	0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
 ☐ (a1) Minors
 ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A number of techniques are used for treating urinary incontinence, including prosthetic sphincters. The present work concerns an entirely intraurethral artificial sphincter that can be implanted without surgery. The valve would be appropriately matched to urethral dimensions, pressures, and flow rates. The prosthetic valve would be potentially useful in cases where a natural valve is either nonopening or nonclosing.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10162-07 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Wound Healing: Biology and Rheology

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

T. L. Talbot, MS	Mechanical Engineer	BEIB, DRS
D. Cromack, M.D.	Surgery	SB, NCI
J. A. Norton, M.D.	Surgery	SB, NCI
G. Solomon, M.D.	Surgery	SB, NCI

COOPERATING UNITS *(if any)*

SB, NCI

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Applied Clinical Engineering Section

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
2.0	2.0	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Preliminary studies have been completed with swine models. These studies involved stamping an indelible grid (10 cm x 10 cm) on the skin of an anesthetized swine, excision of a 1 cm x 10 cm strip of the skin out of the grid area, and approximating the incision edges with silk sutures. Photographs of the grid were taken before excision, after excision, and after suturing. These photographs are being analyzed to determine the impressed strain on the wound closure and eventually relate this information to wound breaking strength (WBS).

Studies based on a rat model that relates biologic and pharmacologic interventions to WBS have been completed. Certain groups were treated pharmacologically during the wound healing process. Significant decrease in WBS was observed in these groups, compared to control groups. Further studies will include the comparison of a tumor-bearing group to control groups.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10163-07 BEI

PERIOD COVERED
October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Magnetoencephalographic Localization of Foci of Neurologic Activity

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

P.D. Smith	Physicist	BEIB, DRS
W.S. Friauf	Section Chief	BEIB, DRS
S. Sato	Neurologist	OCD, NINCDS
D. Rose	Clinical Assoc.	MNB, NINCDS
R. Porter	Deputy Director	NINCDS
E. Dúcla-Soares	Visiting Scientist	MNB, NINCDS
R. Martino	Electrical Engineer	CSL, DCRT

COOPERATING UNITS *(if any)*
Medical Neurology Branch, NINCDS; CSL, DCRT

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electrical and Electronic Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.5	1.5	

CHECK APPROPRIATE BOX(ES)
☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

SQUID (superconducting quantum interference device) magnetometers have been used to study the magnetic activity associated with spike discharges occurring in interictal periods in patients with temporal lobe epilepsy. Magnetic field maps associated with specific spike discharges were obtained from measurements made with the SQUID at various locations on the skull. Improved mathematical models, which accounted for the head shape of the patient, the orientation of the SQUID, and volume current contributions, were developed to calculate the predicted magnetic field maps.

Good agreement was obtained between the experimental clinical maps and those predicted by the model. The model also provided close agreement with the EEG profiles to permit comparison of the localizing accuracy of both the EEG and MEG techniques. A small implantable current dipole source flap was constructed, evaluated, and preliminary clinical data collected. This permits a source to be placed at a known location for evaluation purposes. SQUID instrumentation has been improved with the addition of a shielded room, a gantry support system, and a space digitizer.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10170-07 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Biological Applications of a Computer-Controlled Analytical Electron Microscope

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

R.D. Leapman	Physical Scientist	BEIB, DRS
C.E. Fiori	Physical Scientist	BEIB, DRS
C.R. Swyt	Physiacl Scientist	BEIB, DRS

COOPERATING UNITS *(if any)*

None

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Electron Beam Imaging and Microspectroscopy Group

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS: 0.4	PROFESSIONAL: 0.4	OTHER:

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Experimental measurements have been made on the relative sensitivities of parallel EELS and EDXS for a series of elements commonly encountered in biological microanalysis. The results were compared with theoretically-derived estimates based on scattering cross sections and collection efficiencies. The EELS and EDXS data were collected simultaneously on the Hitachi H700H analytical electron microscope. Energy loss spectra were collected in the second-difference mode to eliminate channel-to-channel gain variations. Multiple least squares fitting of reference spectra was used to quantitate the data. It was shown that EELS can detect not only the light elements with high sensitivity through the K-shell excitation but can also detect elements such as calcium, iron and phosphorus through the L-shell excitation. Sensitivity for calcium is shown to be about three times higher for EELS than for EDXS provided the sample is sufficiently thin. Sensitivities for iron are about the same for the two spectroscopies. Detection limits for phosphorus are about six times lower for EELS than for EDXS.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10184-06 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Physical Chemistry of Biological Macromolecules

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

Marc S. Lewis	Research Chemist	BEIB, DRS
Arun K. Attri	Visiting Scientist	LCB, NHLBI
Michael R. Bubb	Medical Staff Fellow	LCB, NHLBI
Soo II Chung	Research Chemist	LCDO, NIDR
Susan Green	Graduate Student	Dept. Biochem, GU
Preston Hensley	Assoc. Professor	Dept. Biochem, GU
Claude B. Klee	Acting Chief	LMB, NCI
Philip D. Ross	Research Chemist	LMB, NIDDK
Willie F. Vann	Research Chemist	DBP, CBER

COOPERATING UNITS *(if any)*

LCB, NHLBI; LCDO, NIDR; LMB, NCI; LMB, NIDDK; DPB, CBER and Department of Biochemistry Georgetown University

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Microanalysis

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS: 0.6	PROFESSIONAL: 0.6	OTHER:

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of this project is to study the physical properties of a wide variety of biological macromolecules with the goal of correlating these properties to the structure and function of the macromolecules. The emphasis is on the thermodynamics of the interactions of these macromolecules and on their molecular size and shape. Analytical ultracentrifugation and mathematical modeling are the principal research techniques used.

Studies on actin have been directed toward investigating the mechanisms involved in actin polymerization and the interaction of actin with actobindin. Studies on epidermal transglutaminase have involved characterization of proenzyme form and study of the mechanism of activation. Studies on yeast arginase have been directed toward studying the reversible homogeneous association of this enzyme and the role of metal ions in controlling this. Studies on synapsin have involved characterization of the reversible homogeneous association of the various forms of this protein. Studies of various deoxynucleotides have been directed toward investigating the reversible monomer-dimer equilibrium as a function of structure. Studies on the CMP-N-acetylneuraminic acid synthetase gene have involved determination of the nucleotide sequence in the gene and study of some of the physical properties of the encoded enzyme.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

ZO1 RS 10201-05 BE

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Automated Cell-Colony Scanner System

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

Seth Goldstein	Chief, MES	BEIB, DRS
Michael Brownstein	Chief	LCB, NIMH
Zhou Guan Xiong	Visiting Associate	BEIB, DRS

COOPERATING UNITS *(if any)*

Laboratory of Cell Biology, NIMH

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Mechanical Engineering Section

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.1	.1	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A microprocessor-controlled system has been developed to scan tissue culture dishes automatically in order to detect and put scribe marks at the location of fluorescently-labeled cell colonies. Using fluorescein as a label, fluorescence as low as 25% above intrinsic cell background fluorescence can be detected. Small artifacts of selectable size (e.g. 0.2mm) are ignored by the instrument. The fluorescence signal level threshold can be set (e.g. 70% above intrinsic cell background) to within an accuracy of approximately 15% of intrinsic cell background fluorescence and the system will reliably find colonies with a signal exceeding that level. With the above typical values, the number of false positives is typically less than 5 per dish and the time to scan an 80mm diameter tissue culture dish is two to four minutes. This time could likely be reduced somewhat in future versions by redesign of the optical path using a perpendicular rather than oblique laser beam angle of incidence with the moving dish eliminating the requirement for two half scans.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10204-05 BEI

PERIOD COVERED
October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Cell Handling Studies

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

S.B. Leighton	Mechanical Engineer	BEIB, DRS
J.A. Berzofsky, M.D.	Senior Staff	DCBD, NCI

COOPERATING UNITS *(if any)*
DCBD, NCI

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Mechanical Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS: .25	PROFESSIONAL: .25	OTHER:

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

In work on monoclonal antibodies, as well as in other endeavors, it is desirable to be able to isolate individual cells. We are developing an inexpensive device for placing one, and only one cell in each well of a microtitre tray, in culture medium. Thus, the progeny in each well will all be descendents of that single cell, or monoclonal. Our device is an improvement over the existing technique of limiting serial dilution, because each well contains a single cell, while a tray filled by the limiting serial dilution technique will contain many empty wells, and may also contain a few wells that contain two or three cells. The device will be fully automated, requiring minimal operator intervention.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10207-05 BEI

PERIOD COVERED

October 1, 1988 - September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Clinical Engineering Program for the Clinical Center

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

R. Corsey	Electronic Engineer	BEIB, DRS
L. Becich	Executive Officer	DIR CC
M. Evans	Safety Officer	DIR, CC
L. Eldridge	Associate Hospital Administrator	DIR, CC
S. Galen	Associate Hospital Administrator	DIR, CC
J. Wilson	Bldg. Services Manager	DIR, CC

COOPERATING UNITS *(if any)*

Division of Engineering Services, Clinical Care Instrumentation Section, BEIB, DRS

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Applied Clinical Engineering

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
2.0	2.0	0.0

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A clinical engineering program has been provided for the Clinical Center. This program establishes standards and procedures for the hospital such as: (1) fire prevention; (2) calibration of medical equipment; (3) electrical safety; (4) incident (mishap) investigation; and (5) test and evaluation.

Another focus of the program is to participate actively in the formulation of national standards such as the National Electric Code, the Manual for the Safe Use of Electricity in Hospitals, the standards of the Joint Commission on the Accreditation of Health Care Organizations (JCAHO) and the standards of the Association for the Advancement of Medical Instrumentation. A recent initiative is a joint undertaking of a medical equipment management program with the Clinical Care Instrumentation Section, BEIB. This initiative consists of rewriting procedures to satisfy expanded requirements of the Joint Commission. Another facet of this program is the evaluation of computer technology to track equipment expenditures to provide better control of costs.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10210-05 BEI

PERIOD COVERED
June 11, 1988 to July 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Electronic Patient Monitoring System

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

H.E. Cascio	Electronic Engineer	BEIB, DRS
Others:		
G. Hemphill	Engineering Technician	BEIB, DRS
K. Musallam	Head Nurse	NURS, CC
N. Kelly	Administrative Officer	OD, CC

COOPERATING UNITS *(If any)*
CCOD, ARNS

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Electrical and Electronic Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.35	0.15	0.2

CHECK APPROPRIATE BOX(ES)
☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

An electronic patient monitoring system that alerts the nursing staff when a patient (or patients) is leaving the nursing unit is a welcome aid in the care of Alzheimer's Disease patients and other patients with dementia. The system design is based on a wrist watch size radio transmitter to be worn by the patient. A detector unit, placed at the two exit doors, senses the presence of any patient wearing a transmitter watch. With the detection of a patient's transmitter, a microprocessor based controller locks the exiting door, activates an alarm, and displays the patient's name and location on a computer monitor screen. The personal computer records the time and date for each patient's attempt to leave. This data is then used for statistical analysis. A maximum of eight patients can be monitored at two exit doors.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10212-05 BEI

PERIOD COVERED
October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Fluoroimmunoassay Apparatus

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

W.S. Friauf	Chief, EEES	BEIB, DRS
R.L. Berger	Physicist	LTD, NHLBI
G. Hemphill	Electronic Tech.	BEIB, DRS

COOPERATING UNITS *(if any)*
CDC, Atlanta

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electrical and Electronic Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.2	0.1	0.1

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

New rare earth chelate fluorescent probes with decay time constants much longer than the background decay time-constant of typical organic materials offer the potential of a great improvement in sensitivity of time-resolved fluorimetry. However, if they are to rival radioimmunoassay methods the sensitivity requirement becomes so great that overload recovery of the fluorescence detector is a major problem. Extensive past work on this problem is largely inapplicable to the very low speed and level requirements of this situation. Consequently initial effort is being applied to determining the optimum fluorescence detection device and ancillary signal overload limiting circuitry. Problems related to the fluorescent probe at extremely low sample concentrations will be studied in collaboration with CDC, which is interested in this approach as another tool for AIDS research. Finally an evaluation of the details of excitation, optical filtering, and digital signal processing will be worked out and optimized.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10213-05 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Vitreous Fluorophotometry Analysis

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

P.M. Bungay	Chemical Engineer	BEIB, DRS
R.F. Bonner	Biophysicist	BEIB, DRS
M.S. Roy	Ophthalmologist	CB, NEI
M.J. Podgor	Statistician	BE, NEI

COOPERATING UNITS *(if any)*

Clinical Branch, NEI; Off. of Biometry & Epidemiology, NEI

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Chemical Engineering Section

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.0	1.0	

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Vitreous fluorophotometry (VFP) is a clinical procedure for measuring the spatial distribution of fluorescence along the optical axis in a human subject's vitreous following administration of a fluorescent dye. In this project the clinical instrument is a Fluorotron Master manufactured by Coherent, Palo Alto, CA, and the dye is fluorescein sodium given by intravenous injection. The purpose of the project is to improve the protocols for conducting the measurements, processing the output from the instrument, and analyzing the results from the population of normal subjects and patients.

One disease for which VFP may be useful is diabetes and its associated pathology, diabetic retinopathy. Additional goals for this project are to evaluate VFP for use in 1) screening for early detection, and 2) monitoring for treatment efficacy in diabetes and other pathological conditions.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10214-05 BEI

PERIOD COVERED
October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Photoradiation Therapy

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

P.D. Smith	Physicist	BEIB, DRS
R.F. Bonner	Biophysicist	BEIB, DRS
A. Russo	Section Chief	ROB, NCI
T. Delaney	Sr. Investigator	ROB, NCI
H. Pass	Surgeon	SURG, NCI
S. Evans	Clin. Assoc.	SURG, NCI
R. Perry	Clin. Assoc.	SURG, NCI

COOPERATING UNITS *(if any)*
ROB, NCI; SURG, NCI

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electrical and Electronic Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS: 2.5	PROFESSIONAL: 2.5	OTHER:

CHECK APPROPRIATE BOX(ES)
☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Photodynamic therapy (PDT), which is the interaction of light with hematoporphyrin derivative (HDP, Photofrin II), is in clinical use in several areas of application. Currently, PDT is being used clinically for a variety of skin lesions, bronchial obstructions, carcinoma in situ of the bladder, and intraperitoneal tumors. Animal models are being used to assess the potential of using PDT for lung mesothelioma. Specially designed fiber optic probes and introducers were manufactured for all cases, calibrated in terms of irradiance delivered to the tissue. Dosimetry for PDT is complex due to the variable irradiation levels within the tissue, sequestering of HPD, and tissue oxygenation. A plastic replica of a human lung was used to assess the light distribution across the wall for a variety of fiber optic probes and concentrations of light-scattering fluid.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10225-05 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Processing of High Resolution Electron Micrographs

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

Michael Unser	Visiting Associate	BEIB, DRS
Benes Trus	Research Chemist	CSL, DCRT
Alasdair C. Steven	Visiting Scientist	LPB, NIADDK

COOPERATING UNITS *(if any)*

CSL, DCRT and LPB, NIDDK

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Office of the Chief

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.0	1.0	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

High resolution micrographs are often of poor quality, due to a variety of distortions and, especially, a very low signal-to-noise ratio. For micrographs of quasi-periodic arrays or sets of images of ostensibly identical free-standing particles, visual quality can be improved significantly by using correlation-averaging techniques.

We have designed an iterative procedure that compensates for spatial deformation in quasi-periodic crystalline structures and allows noise reduction by averaging. This technique has been applied to the analysis of relaxed skeletal muscle filaments, as well as to filaments in a state of rigor.

We have conducted an objective comparison of various normalization techniques and factorial representations. We found that the use of Principal Components Analysis together with a mean/variance normalization is the most favorable approach.

We have improved the computational efficiency of the spectral signal-to-noise ratio (SSNR) resolution criterion by extending it for partial averages. In this approach, the initial data set is randomly partioned into a given number of subsets, each subset is separately averaged, and a reduced form of the SSNR is computed over successive concentric annuli in Fourier space with increasing radial frequencies.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10238-04 BEI

PERIOD COVERED
October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Automation of BEIB Information Processing Functions

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

J.R. Ellis	Expert	BEIB,DRS
C. Martin	Management Analyst	MAO, DRS
C.C. Gibson	Electronics Engineer	BEIB, DRS
R.L. Levin	Biomedical Engineer, MES	BEIB, DRS
M.E. Gavin	Management Assistant	BEIB, DRS

COOPERATING UNITS *(if any)*

DRS, MAO and DCRT, CSL

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Office of the Chief

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS: 1.0	PROFESSIONAL: 0.5	OTHER: 0.5

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
 ☐ (a1) Minors
 ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The computational and accounting resources of the branch are often inadequate to the demands placed on them. The objectives of this project are: to determine the needs of the branch; to identify appropriate resources; and to match resources to changing user demands.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10240-04 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Clinical Measurement of Microvascular Blood in Sickle Cell Patients

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

E.C. Walker	Chief, ACES	BEIB, DRS
G.P. Rodgers	Robert Wood Johnson Fellow	LCB, NIDDK
A.N. Schechter	Chief	LCB, NIDDK

COOPERATING UNITS *(if any)*

LCB, NIDDK

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Applied Clinical Engineering Section

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.5	0.5	

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

It is commonly known that sickle cell patients possess red blood cells that have abnormal rheological properties. The cell properties affect bulk vascular flow in general and microvascular flow in particular. Severe manifestations of this disease can be observed acutely, during intensely painful crises, and chronically, as demonstrated by damage to the cardiovascular system and various organs. It is our intention to develop and explore the use of non-invasive instrumentation to study the character and degree of peripheral blood flow in stable sickle cell patients. We are currently using commercial devices to monitor non-invasively several variables. Because the devices we employ are relatively new, we will also develop a reliable means for evaluating them for potential use with our patient population.

Flow studies of this nature can lead to improved understanding of the micro-obstructive component of sickle cell disease as well as serve to evaluate potential therapies such as hydroxyurea.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER ZO1 RS 10248-04 BEI

PERIOD COVERED
October 1, 1988 - September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Intra-arterial Optical Evaluation

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

P.D.Smith	Physicist	BEIB, DRS
Others		
M.B. Leon	Cardiologist	CB, NHLBI
R. Neville	Clinical Assoc.	CB, NHLBI

COOPERATING UNITS *(if any)*
NHLBI, MCM LABS

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Electrical and Electronic Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS: 1.0	PROFESSIONAL: 1.0	OTHER:

CHECK APPROPRIATE BOX(ES)
☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Evaluation of the intra-arterial wall surface is necessary for control of laser ablation of tissue. Angioscopy produces clear observation of the target sites, provided adequate irrigation of the vessel with saline solution is maintained. Precise quantitative location of the target is difficult. In addition, size constraints may limit angioscopy's usefulness in the coronary vessels.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10252-03 BEI

PERIOD COVERED
October 1988 - September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Physiological Monitoring System for Sepsis Models

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

E. C. Walker	Chief, ACES	BEIB, DRS
R. Corsey	Electronic Engineer	BEIB, DRS
B. Shepard	Clinical Associate	SURG, NCI
J. A. Norton	Section Chief	SURG, NCI

COOPERATING UNITS *(if any)*
SURG, NCI

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Applied Clinical Engineering

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1	1	

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

For studying the role of cachectin (Tumor Necrosis Factor -TNF) in septic shock we have developed a physiological monitoring system for laboratory rats. Temperature and direct arterial pressure were monitored.

Special carotid/aortic catheters were designed and tested for frequency response. During actual studies septic shock was induced and physiologically characterized.

Preliminary results show that findings based on assayed values of TNF are inconclusive and that additional approaches may be warranted.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10256-03 BEI

PERIOD COVERED

October 1, 1988 - September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Mechanical Prosthetic Heart Valve Tester

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

T. L. Talbot	Mechanical Engineer	DRS, BEIB
F. A. Arabia	Senior Investigator	SB, NHLBI
R. E. Clark	Chief	SB, NHLBI
S. F. C. Stewart	Staff Fellow	SB, NHLBI

COOPERATING UNITS *(if any)*

Cardiac Surgery Branch, NHLBI

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Applied Clinical Engineering

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.5	1.5	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Six different manufacturers' prosthetic heart valves were tested and ranked according to performance indices described by W. Swanson and S. Gabbay. Additionally, a technique was devised whereby the pressure drop across the aortic valve could be predicted by velocity measurements made with continuous wave Doppler (CWD) imaging. The results of preliminary *in vitro* studies demonstrate a high correlation (r>0.9) between the peak velocity as measured with CWD and the predicted velocity obtained by the application of a simplified Bernoulli equation, which uses a measured maximum pressure drop across the aortic valve. Also, an acoustical signature analysis technique is under investigation for possible non-invasive detection of partially-failed single leaflet type mechanical valves.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10257-03 BEI

PERIOD COVERED

October 1, 1988 - September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Analysis of Propagation of Light in Turbid Biological Tissues

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

R. F. Bonner	Physicist	BEIB, DRS
R. Nossal	Senior Research	LPS, DCRT
G. Weiss	Chief	LPS, DCRT
S. Havlin	Visiting Scientist	LPS, DCRT
T. Delaney	Senior Investigator	ROB, NCI
M. Leon	Senior Investigator	CB, NHLBI

COOPERATING UNITS *(if any)*

LPS, DCRT; Department of Physics, Bar-Ilan University, Israel

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Electrical and Electronic Engineering Section

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.0	1.0	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Many of the clinical research projects of the laser biophysics group involve the interaction of light with tissue (e.g., laser microsurgery, laser Doppler blood flow measurements, photodynamic therapy of cancer, noninvasive platelet assessment). In order to quantitate these techniques more fully, we have undertaken theoretical modeling of light propagation in biological tissues and turbid media.

Analytical equations have been devised characterizing various parameters of photons illuminating a tissue surface (including probability of surface re-emission at a given distance, mean path before re-emission, mean depth of penetration, probability of absorption with depth). These expressions have been used to interpret empirical measurements on living tissues and to quantify better a variety of clinical measurements (e.g., laser Doppler blood flow and volume measurements, dosimetry in PDT of cancer, and remote sensing of atherosclerotic plaque.

Recently our theoretical predictions of path length distributions of re-emitted photons have been applied to temporal dispersion of picosecond laser pulses in brain and muscle. Such analysis allows absolute quantitation of hemoglobin and myoglobin oxygen saturation *in vivo*.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10258-03 BEI

PERIOD COVERED

October 1, 1988 - September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Photochemical Inactivation of Virus and Bacteria in Blood

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

R. F. Bonner	Physicist	BEIB, DRS
K. N. Prodouz	Biologist	DBBP, FDA
J. C. Fratantoni	Section Chief	DBBP, FDA
A. Russo	Section Chief	ROB, NCI

COOPERATING UNITS *(if any)*

DBBP, FDA; ROB, NCI

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Electrical and Electronic Engineering Section

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1	1	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Photochemical sterilization of blood products is the ultimate goal of this project, in which we are quantitating photochemical destruction of virus in blood and blood products and the effects of the process on the native blood components. Initial studies using an XeCl excimer laser characterized the response of virus and blood components as functions of cumulative fluence and peak irradiance. Single and multiple photon photochemical schemes were investigated. Single photon photochemistry resulted in an efficacious treatment range between 10-20 J/cm^2 in which a hardy virus is inactivated and platelets and plasma proteins are minimally affected. Multiple photon effects at higher irradiance led to increased protein damage in blood components without increasing efficacy of viral inactivation. Augmentation of this therapeutic window by photochemistry using exogenous agents such as riboflavin, tetracycline, and hemocyanin was investigated with a focus on the adverse effects on platelets and the relative susceptibility of different viruses dependent on the complexity of their coat. The inhibitory effect of serum and albumin on photochemistry was also examined. Proposed work will examine exogenous agents which show strong affinity for binding to DNA and thereby might increase therapeutic efficacy.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10259-03 BEI

PERIOD COVERED

October 1, 1988 - September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Visual Target Tracking-Ability Assessment System

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

T. R. Clem, Sr.	EEES	BEIB, DRS
R. Litman, M.D.	CNSB	NIMH
T. P. Zahn, M.D.	LPP	NIMH

COOPERATING UNITS *(if any)*

CNSB, LPP, NIMH

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Electrical and Electronic Engineering Section

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1	0.9	0.1

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Abnormal eye movements found in CNS diseases may be related to the underlying pathophysiology of a particular CNS disease. Although the oculomotor nuclei, their descending primary motor neurons, and the extraocular muscles they innervate ultimately mediate eye movements, higher centers, including premotor areas in the brainstem, midbrain, subcortical areas and cerebral cortex, are also involved in the movements. The oculomotor nuclei and neurons, together with the higher motor centers, functionally comprise five oculomotor systems responsible for different types of eye movements. Of these, the smooth pursuit eye movement system and saccadic eye movement system are of interest, for they seem to be abnormal in CNS disorders where disease in higher subcortical and cortical centers is implicated.

Both smooth pursuit and saccadic eye movements have properties that clearly distinguish them and make them easy to measure. Disorders of smooth pursuit eye movements (SPEM) have been found in schizophrenia, as well as other psychiatric disorders characterized by psychotic symptoms. Abnormal SPEM can be found in a variety of CNS illnesses, primarily those that affect the oculomotor nuclei (e.g. brainstem infarction). Abnormal SPEM and abnormalities in saccadic eye movements have also been associated with more diffuse brain diseases such as DAT, Huntington's and Parkinson's Diseases.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10260-03 BEI

PERIOD COVERED

October 1, 1988 - September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Real-Time High-Performance Confocal Laser Scanning Optical Microscope

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

S. Goldstein	Chief, MES	BEIB, DRS
M. Datiles	Clinical Branch	NEI
T. Smith	LNP	NINDS

COOPERATING UNITS *(if any)*

Clinical Branch, NEI

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Mechanical Engineering Section

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.8	0.7	0.1

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A no-moving-parts, 30 frames per second, laser beam scanning confocal reflected light microscope has been developed. In principle the technique can be extended to fluorescence and transmission light microscopy. Acousto-optic beam deflectors, controlled by all digital electronics, move a laser beam in a 512 line interlaced 8.5mm square raster. The light enters an inverted microscope through the side camera port, and is imaged at the object by the microscope objective. Reflected light returns through the objective, out the camera port, through a beam splitter, and is imaged onto the photocathode of an Image Dissector Tube (IDT). Confocality is provided by raster scanning the IDT aperture coincident with the congruent image of the laser beam incident on the object. Real time jitter-free reflected light images of a variety of biological objects have been produced. Computer controlled alignment of the laser scan and IDT is performed in several seconds.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10267-03 BEI

PERIOD COVERED
July 30, 1988 - July 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
A Low-Noise Electrometer for an Automated Hemoglobin Oxygen Equilibrium Curve Measurement System

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

H. E. Cascio	Electr. Eng.	BEIB, DRS
R. L. Berger	Physicist	LTD, NHLBI
K. O. Kalmbach	Eng. Tech.	LTD, NHLBI

COOPERATING UNITS *(if any)*
LTD, NHLBI

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Electrical and Electronic Engineering

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, Maryland 20892

TOTAL MAN-YEARS: 0.8	PROFESSIONAL: 0.4	OTHER: 0.4

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Measurement of the hemoglobin oxygen equilibrium curve (OEC) in an automated system is hampered by noise. To obtain reliable results in reading partial pressures with an accuracy of 0.01 mmHg requires special techniques in electronic circuit design. The pO_2, pH, and the pCO_2 electrodes have very high internal resistance with very low output signal levels. When these devices are used in an environment contaminated by radio frequency interference (RFI) from a computer, the magnetic fields of stepping motors, as well as power line transients generated by a high current water bath, the electrode output leads must be kept short and shielded. The electrode signals must be kept scaled and offset by a computer-controlled signal processor that properly interfaces these voltages to an AT-type personal computer, for further software analysis. Another task to be performed is the designing and fabrication of the required circuitry for the development of the automated system to perform the desired measurements.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10270-03 BEI

PERIOD COVERED

October 1, 1988 - September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Computer-Assisted Analysis of M-Mode Echocardiograms

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

M. Unser	Visiting Associate	BEIB, DRS
M. Eden	Chief	BEIB, DRS
G. Pelle	Chargé de Recherche	Unité 138, INSERM
P. Brun	Chief	Unité 138, INSERM

COOPERATING UNITS *(if any)*

Unité 138, INSERM

LAB/BRANCH

Office of the Chief

SECTION

Biomedical Engineering and Instrumentation

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.0	1.0	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Echocardiography is a non-invasive method for monitoring ventricular function and evaluating myocardial hypertrophy in patients with heart disease. Although the information displayed in two-dimensional echocardiograms is generally the most useful for diagnostic purposes, one-dimensional or M-Mode echocardiography, due to its greater reliability, is widely accepted as the reference method for the evaluation of myocardial wall thickness.

We have developed two algorithms for the processing of M-mode echocardiograms and implemented those on a Macintosh II work station. The first allows an automated extraction of myocardial borders. The second performs a restoration of sequences of several consecutive heart beats by performing an average with respect to a normalized time-scale. The essential feature of this technique is to compensate in a fully automated way for variations of the heart rate.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10271-02 BEI

PERIOD COVERED
October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Strain Rate Dependency of Wound Breaking Strength

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

T. L. Talbot, M.S.	ACES	BEIB, DRS
D.T. Cromack, M.D.		NCI, SB
J. A. Norton, M.D.	Chief	NCI, SB

COOPERATING UNITS *(if any)*
Surgery Branch, NCI

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Applied Clinical Engineering

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.25	0.25	

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This section has been involved in wound healing studies for the past decade. The primary measurement which these studies make is the wound breaking strength of a dermal wound at various stages of the healing process. Multiple modalities and healing interventions have been employed which were hoped to enhance the healing of normal wounds or to minimize the deleterious effects on healing which many chemotherapeutic agents effect. Currently there is a burgeoning amount of research in the area primarily as a result of the availability of relatively low cost growth factors that have been synthesized through the employment of recombinant techniques. Unfortunately, cross-study comparisons are difficult to interpret because of the strain rate dependency of the wound breaking strength. The literature has reported extension rates varying from one to thirty centimeters per minute.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10272-02 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Photometry for Photo-Dynamic Therapy

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

W.S. Friauf	Chief, EEES	BEIB, DRS
Others:		
J. Cole	Elect. Engr.	BEIB, DRS
P.D. Smith	Physicist	BEIB, DRS
R.F. Bonner	Biophysicist	BEIB, DRS
A. Russo	Section Chief	ROB, NCI
T. Delaney	Clinical Assoc.	ROB, NCI
H. Pass	Surgeon	SURG., NCI

COOPERATING UNITS *(if any)*

ROB, NCI, and SURG, NCI

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Electrical and Electronic Engineering Section

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.4	0.4	

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Dosimetry for photodynamic therapy (PDT) involves measurement of hematoporphyrin derivative (HPD) concentration, oxygen concentration, singlet oxygen concentration, and therapeutic light level, all as a function of position throughout the tissue being treated intentionally or unavoidably. Non-invasive measurements are essentially limited to surfaces, although theoretical and empirical models can be used to estimate values some distance into the tissue. Fiber optic probes can be used for direct sub-surface measurements.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10274-02 BEI

PERIOD COVERED

October 1, 1988 - September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

A Non-invasive Method to Measure Tissue Stress

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

Peter Basser, Ph.D.	Staff Fellow, MES	BEIB, DRS
John Eng	Hughes Fellow	LKEM, NIHLB
Robert Balaban, Ph.D.	Section Chief	LKEM, NIHLB

COOPERATING UNITS *(if any)*

SN/NINCDS

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Mechanical Engineering

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.2	0.2	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Elevated levels of mechanical stress can reduce tissue perfusion by collapsing arterioles and capillary beds. However, lower levels of mechanical stress are known to stimulate growth of bone and cartilage. Measuring and monitoring this stress is the purpose of a device that is under development in BEIB. The contact stress* sensor consists of a flexible bag containing a polyelectrolyte gel and an NMR pH indicator. Normal stress applied to the bag is transmitted to the spongy gel, squeezing interstitial fluid into the surrounding bath. Compressing the gel increases its charge density, forcing a new intracellular and extracellular equilibrium pH distribution. The applied stress is inferred from a non-invasive NMR spectroscopic measurement of pH. Since no external connections are required, it is expected that a sterile field can be maintained. In addition, a potential exists for long-term stability. The sensor contains no cytotoxic substances or non-toxic chemicals in non-physiologic concentrations whose release would also present a threat to surrounding biological tissue. The stiffness of the gel can be changed by altering its polymer content allowing the operating range and sensitivity of the sensor to be controlled.

*N.B. Contact pressure is defined as the normal component of the interfacial stress between two bodies in contact with one another; it is not the ambient isotropic normal stress known as hydrostatic pressure.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10275-02 BEI

PERIOD COVERED
October 1, 1988 - September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
A Method to Measure Mechanical Constants of a Hydrogel

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

Peter Basser, Ph.D.	Staff Fellow, MES	BEIB, DRS
Piero Chiarelli, Dott.	Visiting Fellow, MES	BEIB, DRS

COOPERATING UNITS *(if any)*
None

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Mechanical Engineering

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.7	0.7	

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A method has been developed to measure rapidly and accurately three important material constants of a hydrogel sample. The shear modulus, m, the bulk modulus, k, and the hydraulic permeability, 1/f, can be determined from a single stress relaxation experiment. The material constants are treated as free parameters whose values are optimally estimated by minimizing the variance between predicted and empirical force relaxation waveforms. Values of the three constants obtained by this method agree with values obtained by independent free-swelling and permeability measurements.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10276-02 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Microdialysis Probe Studies

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

R.L. Dedrick	Chemical Engineer	BEIB, DRS
P.F. Morrison	Physical Scientist	BEIB, DRS
P.M. Bungay	Chemical Engineer	BEIB, DRS
B.A. Ball	Chemical Engineer	BEIB, DRS
K.H. Dystra	Chemical Engineer	BEIB, DRS
J.K. Hsaio	Psychiatrist	LCS, NIMH
I.N. Mefford	Chemist	LCS, NIMH
K.S. Bankiewicz	Neurosurgeon	SNB, NINCDS

COOPERATING UNITS *(if any)*

Lab. Clinical Science, NIMH; Surgical Neurology Br., NINCDS

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Chemical Engineering Section

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.5	1.5	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Microdialysis probe technology provides a means for sampling diffusible tissue extracellular constituents. However, the relationship of the probe effluent concentrations to their tissue counterparts is a complex function of solute molecular weight, solute physicochemical properties, tissue properties, probe membrane properties, probe geometry and perfusion rate, and the trauma of probe insertion into the tissue. These dependencies will be studied in order to improve the quantitative usefulness of the technology. The focus of applications is the brain in connection with Parkinson's disease and transplant therapy. Solutes of particular interest are dopamine and its metabolites. Approaches considered include mathematical modeling of solute transport within the probe and surrounding medium with both *in-vitro* and *in-vivo* validation experiments.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10277-02 BEI

PERIOD COVERED

July 30, 1988 - July 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Technical Assistance for Television Use In Research

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

H. E. Cascio	Electr. Eng.	BEIB, DRS
P.D. Smith	Physicist	BEIB, DRS
S. Stanhope	Biomechanics Laboratory	CC

COOPERATING UNITS *(if any)*

Biomechanics Laboratory, CC

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Electrical and Electronic Engineering

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.2	0.2	

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Television systems have become an integral part of many scientific and medical research studies at the NIH. The implementation of a television system demands adherence to rigid standards for system interconnections and adjustments. On request, EEES, BEIB provides technical assistance such as system design and consultation is provided to the Intramural Research Program. Consultations range from assistance in selecting system components such as cameras, associated electronics, and lenses to solving problems of an existing system. A typical example is represented by the requests of Dr. Steven Stanhope.

Dr. Stanhope has a Vidicon six camera computer operated motion analysis system for the acquisition and evaluation of data associated with patient function. The video system detects the presence of reflective markers located on the patient and by software, calculates the three dimensional location of each marker. The problems with persistence, blooming, and electronic stability of the vidicon makes the balancing of the six cameras very difficult. The solution is to replace the vidicon cameras with CCD cameras. The CCD cameras have superior electronic stability and do not display picture smearing when detecting fast motion.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10283-02 BEI

PERIOD COVERED
October 1, 1988 - September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
A Micro-Computer Based Flow Cytometry Data Collection and Analysis System

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

C.P. Mudd	Biomedical Engineer	ACES, BEIB, DRS
J. A. Dvorak	Researcher	LPD, NIAID

COOPERATING UNITS *(if any)*
LPD, NIAID

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Applied Clinical Engineering

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.1	0.1	0.0

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Traditionally, minicomputers have been used for the collection and analysis of data generated by flow cytometers. One reason is that, until recently, microcomputers, which would be more cost-effective alternatives, were not sufficiently developed to satisfy the unique demands imposed by flow cytometers. In order to overcome some of the deficiencies of early generations of microcomputers, several of the functions required for data collection, such as analog to digital conversion and data storage in static RAM have been performed "external" to the computer which was used for the data analysis. In addition, "mixed" flow cytometry systems in which data are collected with a minicomputer and analyzed with a microcomputer have been developed. However, these approaches are not cost effective and do not effectively use the improved capabilities of available microcomputers. With the evolution of the Intel 80XXX family of processors, reliable peripherals, and a variety of powerful compilers, it has become feasible to develop a relatively inexpensive microcomputer-based data collection and analysis system for flow cytometry that performs as well as, or better than, minicomputer-based systems.

Earlier we developed an electronic interface system which linked the analog signals from the four preamplifiers of the flow cytometer to the micro-computer. This system collected, processed, and conditioned the analog signals before acquisition by the micro-computer and effectively solved the problem of interfacing asynchronous and synchronous data conversion, acquisition and storage. The complete system, flow cytometer, interface, and micro-computer, has been in routine laboratory use for almost eight months.

During this period, we have observed a small asymmetry in the acquired histograms. The cause was traced to the simultaneous occurrence of an analog pulse from the flow cytometer and the reset of the interface system. If the interface system completes reset while an analog pulse is present, the integrators were triggered and integrated the remaining portion of the pulse. These integrated pulses were always smaller than a fully integrated pulse. When the smaller values were added to the normal values, the histogram was skewed down toward the lower values. The problem is most severe at high flow rates.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10284-02 BEI

PERIOD COVERED

October 1, 1988 - September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Measurement of the Binding Heats of Oxygen to Hemoglobin

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

C.P. Mudd	Biomedical Engineer	ACES, BEIB, DRS
R.L. Berger	Chemist	LTD, NHLBI

COOPERATING UNITS *(if any)*

LTD, NHLBI

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Applied Clinical Engineering

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.1	0.1	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The binding of oxygen to hemoglobin is thought to be a multistep process with different rate constants for each step. With an all tantalum stopped-flow calorimeter developed earlier, we can easily measure the heat of binding of oxygen to hemoglobin. The all-tantalum system will prevent the diffusion of oxygen into the system and will allow us to measure these heats over the entire saturation range, 0-100%; preliminary measurements of the binding heat at 50% saturation are in good agreement with published values.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10285-02 BEI

PERIOD COVERED

October 1, 1988 - September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Determination of Binding Enthalpies of Anthracycline Drugs to DNA Host Cells

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

C.P. Mudd	Biomedical Engineer	ACES, BEIB, DRS
D.P. Remeta	Research Fellow	FDA
K.L. Breslauer	Chemist	Rutgers University

COOPERATING UNITS *(if any)*

Department of Chemistry, Rutgers University

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Applied Clinical Engineering

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.1	0.1	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The first preliminary set of measurements of the drug binding enthalpies for daunomysin to DNA in the 10-20 micromolar range (where the monomeric form predominates) have been made. These results were presented in a poster session at the 1988 meeting of the Biophysical Society. The enthalpies at these concentrations were in the 30-50 microjoule range. With a tantalum stopped flow calorimeter, we were able to measure 120 of these reactions per day with an uncertainty of only 3 microjoules. We anticipate two more sets of experiments to explore the salt and temperature dependence of the enthalpies. The experiments are being performed in collaboration with the Bureau of Biologics of the FDA.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10286-02 BEI

PERIOD COVERED

October 1, 1988 - September 30, 1989

TITLE OF PROJECT *(80 characters or less Title must fit on one line between the borders.)*

High Speed Differential Stopped Flow Calorimeter

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

C.P. Mudd	Biomedical Engineer	ACES, BEIB, DRS
R.L. Berger	Chemist	LTD, NHLBI

COOPERATING UNITS *(if any)*

LTD, NHLBI

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Applied Clinical Engineering

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.1	0.1	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A preliminary single channel, high speed, stopped-flow calorimeter has been constructed to evaluate mixing speeds, flow velocities, pressure drops, and thermal detection sensitivity. The system uses a variable speed flywheel and electrically actuated clutch to transfer sufficient energy to the two drive syringes to mix reagent volumes of 200 microliters in 10 milliseconds or less. The inlet tubes from the drive syringes, as well as the mixer and the detection chamber are kept at constant temperature between 25 and 50 deg C. An ultra-fast thermistor (1 ms) is located in the detection chamber to measure the temperature rise during the reaction. The detection chamber also contains a quartz observation tube for optical measurement of the reaction.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10289-02 BEI

PERIOD COVERED

October 1, 1988 - September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Tantalum Batch Calorimeter for *In Vitro* Cell Studies

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

C.P. Mudd	Biomedical Engineer	ACES, BEIB, DRS
R.L. Berger	Chemist	LTD, NHLBI

COOPERATING UNITS *(if any)*

LTD, NHLBI

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Applied Clinical Engineering

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.1	0.1	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

In biological experiments, it is often desirable to monitor the heat output of in vitro cell preparations as nutrients, drugs, etc., are added to the preparation. In addition, the measurement of temperature, p02, pC02, and pH is very useful. To meet these needs, we have designed a new type of heat conduction batch calorimeter. The instrument has two, large (5 ml) tantalum cells arranged in a differential configuration. Each cell has provision to accommodate 6, 1 mm O.D. fluid delivery lines or fiber optic sensor lines. The heat production of the cell preparation is detected using a scheme similar to that used in our earlier batch calorimeters. The cell temperature can be set between 4 deg C and 50 deg C.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10296-02 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Experiments with a High Resolution Field-Emission STEM

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

R.D. Leapman	Physical Scientist	BEIB, DRS
C.E. Fiori	Physical Scientist	BEIB, DRS
C.R. Swyt	Physical Scientist	BEIB, DRS
S.B. Andrews	Chemist	LN, NINCDS
J. Hunt	Electronics Engineer	Lehigh Univ.
B. Ciliax	NRC Fellow	BEIB, DRS

COOPERATING UNITS *(if any)*

LN, NINCDS; Lehigh University

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Electron Beam Imaging and Microspectroscopy Group

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.8	0.8	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The Vacuum Generators cryotransfer sample stage was found to be mechanically and thermally stable at temperatures below -175° C, and provides a very clean specimen environment under these conditions: no significant ice contamination was found to be present at low temperatures. Tests were carried out demonstrating the feasibility of imaging hydrated ice-embedded microtubule and virus preparations. The Tracor Northern ultrathin window x-ray detector was shown to detect the light elements (boron, carbon, nitrogen, oxygen and fluorine) although the peak shapes were complicated by effects of the pulse processor. The solid angle of 0.18 steradians subtended by the EDXS detector yielded a strong spectral signal from a test sample of freeze-dried cryosections of isolated nerve terminals (synaptosomes). The Gatan parallel-detection electron energy loss spectrometer was interfaced to the HB501 after modifications had been made to allow for a high temperature bake-out. In addition an extra ion pump was added for ultrahigh vacuum compatibility. The spectrometer energy resolution was demonstrated to be 0.35 electron-volts, as limited by the energy width of the field-emission distribution. A PC-AT computer system was employed to obtain parallel electron energy loss maps from ferritin molecules to demonstrate the capability of high spatial resolution microanalysis in the STEM.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10298-02 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Optical Assessment of Tooth Vitality

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

J. Schmitt	Staff Fellow	BEIB, DRS
R. Webber	Chief (now retired)	NIDR, DSB
U. Ruttimann	Chief	NIDR, DSB
M. Tsuchimochi	Visiting Researcher	NIDR
W. Engelke	Visiting Researcher	NIDR
E.C. Walker	Section Chief	BEIB, DRS

COOPERATING UNITS *(if any)*

NIDR, DSB

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Applied Clinical Engineering Section

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.5	0.4	0.1

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

We have developed noninvasive plethysmographic techniques for determining the status of the blood circulation in the dental pulp. By detecting minute changes in the intensity of light scattered by the tooth during systole, the vitality of a tooth can be established unequivocally. Preliminary results indicate that the oxygen saturation (S02) of blood in the pulp can be estimated from intensities scattered from the tooth at three wavelengths. Theoretical results and preliminary data obtained from both *in vitro* and *in vivo* experiments suggest that the use of these plethysmographic methods for routine assessment of tooth vitality in the clinic is feasible.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10299-01 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Elevated Pressure, Biologically Contained Flow Cell

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

T.L. Talbot	Mechanical Engineer	BEIB, DRS
C. Mudd	Biomedical Engineer	BEIB, DRS
J. Dvorak	Senior Investigator	LP, NIAID

COOPERATING UNITS *(if any)*

NIAID, Laboratory of Paracytology

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Applied Clinical Engineering Section

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.5	0.25	0.25

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The flow cell currently used by this lab for flow cytometry studies was designed for lower pressures than are presently required by the biological restraints of the organisms now being studied. Additionally, these organisms are live parasites that require suitable biological containment.

These parasites, T-Cruzi, are potentially lethal and do not respond to any known medications. Therefore, a new flow cell must be designed specifically for this application which will insure the safe operation and the scientific integrity of the flow cytometer.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10300-01 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Myocardial Cell Contractility Study

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

T. Talbot	Mechanical Engineer	BEIB, DRS
C.P. Mudd	Biomedical Engineer	BEIB, DRS
Joseph Schmitt	Staff Fellow	BEIB, DRS
G. Krishna	Sr. Investigator	CP, NHLBI

COOPERATING UNITS *(if any)*

NHLBI, Clinical Pharmacology

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Applied Clinical Engineering Section

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
2.0	2.0	0.25

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Myocardial cells which are grown in culture exhibit dramatic visible changes in beating characteristics when they are presented with various types of chemotherapeutic agents. A technique for quantifying these changes is of paramount importance. Because of the fragile nature of these cells in culture the measurement modality must be totally non-invasive.

A video tracking system which is currently used to quantify the myocardial depressant effects of septic serum on rat neonate myocardial cell cultures will be adapted to this experimental setup. This system can measure the displacement of an individual cell as it beats. We intend to enhance this system by adding the first and second derivatives which will yield the velocity and acceleration of the beating cell. It is hoped that the acceleration can be incorporated into an estimate of the force of contraction.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10301-01 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Particle Size Distributions of Nebulized Drugs

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

E.C. Walker	Chief, ACES	BEIB, DRS
A. Rich	Mechanical Engineer	BEIB, DRS
R.C. Hubbard, MD	Senior Investigator	PB, NHLBI

COOPERATING UNITS *(if any)*

PB, NHLBI

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Applied Clinical Engineering Section

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.08	0.08	

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Recombinant alpha 1-antitrypsin is currently administered intravenously in the treatment of cystic fibrosis. A new protocol has been designed to treat these patients via aerosol so as to deliver large doses of alpha-1 antitrypsin directly to the respiratory tract.

We will study the particle size distributions of several nebulizers to ensure that the proper particle size (1-3 microns) is being delivered to the patient.

The Misty, Retec, and Vortran nebulizers will be evaluated using a commercially available instrument such as the Malvern, TSL, or In-Tox particle sizer.

In the future, the size distribution of other aerosolized drugs will be evaluated for patient therapy.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10302-01 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Calibration System for Electronic or Automated Sphygmomanometers

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

E.C. Walker	Chief, ACES	BEIB, DRS
T. Carson	Technician	BEIB, DRS
R. Corsey	Electronic Engineer	BEIB, DRS

COOPERATING UNITS *(if any)*

L. Eldridge Clinical Center

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Applied Clinical Engineering Section

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS: 0.3	PROFESSIONAL: 0.3	OTHER:

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Current hospital accreditation standards require performance evaluation of hospital equipment. Although certain performance aspects of electronic sphygmomanometers can be evaluated, a standardized complete evaluation is not commercially available.

We are currently developing a system to simulate a subject during the blood pressure measurement cycle. This system will serve as a standard "patient" for the evaluation of electronic sphygmomanometers. In practice, a user will be able to interface an electronic sphygmomanometer to the calibrator and select the values, such as blood pressure and heart rate, which the sphygmomanometer is to be tested at. At the conclusion of the test a summary report will be provided.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10303-01 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Assessment of Scratching in Biliary Cirrhosis Patients

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

T. Talbot	Mechanical Engineer	BEIB, DRS
J. Schmitt	Staff Fellow	BEIB, DRS
E. Walker	Section Chief	BEIB, DRS
N. Bergasa	Medical Staff Fellow	LDS, NIDDK
E. Jones	Senior Investigator	LDS, NIDDK

COOPERATING UNITS *(if any)*

NIDDK, Liver Unit

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Applied Clinical Engineering Section

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.0	1.0	

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Patients with the disease primary biliary cirrhosis suffer from severe bouts of itching which is manifested clinically by chronic scratching. In order to evaluate the efficacy of experimental drugs that may relieve the itching, it is necessary to somehow quantify the patient's scratching. A piezoelectric foil cemented to the patient's primary scratching fingernail will transduce mechanical vibrations generated by the scratching to a miniature FM transmitter. After the signal is obtained with a FM receiver, it will be processed by a custom designed frequency counter which in turn is interrogated and reset periodically by a personal computer. The study will consist of measurement periods of six to eight hours both before treatment and after treatment with specific drugs. Each patient will serve as his or her own control.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10304-01 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Biphasic *In-Vitro* Heart Cell Pacer

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

T. Talbot	Mechanical Engineer	BEIB, DRS
J. Schmitt	Staff Fellow	BEIB, DRS
J. Parrillo	Chief, ICU	CC, CRM

COOPERATING UNITS *(if any)*

CC/CRM

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Applied Clinical Engineering Section

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.2	0.5	1.5

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Myocardial cells in culture require comparatively high currents to pace the cells effectively at physiological rates. At these high currents, standard monophasic pacers cause severe electrolysis of the pacing electrodes. This problem was overcome by the design and implementation of a biphasic pacemaker.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10305-01 BEI

PERIOD COVERED
October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
CC Image Management System

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

R.L. Levin	Biomedical Engineer	BEIB, DRS
E. Lamoreaux	Computer Scientist	ROB, NCI
J. Foy	Asst. Chief	MIS, CC
T. Lewis	Chief	MIS, CC

COOPERATING UNITS *(if any)*
Radiation Oncology Branch/NCI; Medical Infor. System Dept./CC

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Mechanical Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.0	1.0	

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

In order to facilitate the viewing and analysis of biomedical images, the Clinical Center is in the process of designing and developing an Image Management System (IMS) to complement the current text-based Medical Information System (MIS). This new system will consist of the following four key components: (1) several different types of medical image gateways (MIG), (2) an image archival and retrieval system (IARS) that has a MIS interface, (3) several different types of workstations (WS) possessing a common biomedical shell, and (4) an interconnecting communications network. The MIGs will permit digital radiological images (i.e. MR, CT, PET, etc.), non-digital radiological images (i.e. plane-film X-ray), and non-radiological images (i.e. video-microscopic images, EKG tracings, patient monitor information etc.) to be converted to a common format, compressed in a loss-less manner, and automatically sent to the IARS. The IARS will permit not only the long term archiving on optical media of the images coming from the MIGs but also the retrieval of multiple modality images to local workstations in response to queries via the existing MIS data-base, the new IMS data-base, or individual departmental data-bases. In the workstation area, we will be developing two or three different types of biomedical workstations. The first is a low-cost WS that is capable of seamlessly accessing both MIS and IMS, that is, display both MIS-based text imformation and IMS-based images, and would be sufficiently cost effective to replace the current MIS units throughout the CC. This low-end WS could be based upon a stripped PC or, possibly, an X-windows terminal. The second type of WS is a medium range unit that would be suitable for the desktop of a physician, scientist, etc. This unit, will probably be based upon a Mac II and would serve the needs of its owner (e.g. word processing, spreadsheets, etc.) by having some local processing and disk storage capability in addition to being able to access both MIS and IMS. It will have image processing power to the extent that images from multiple modalities can be extensively manipulated in 2-D (i.e. window, level, zoom, pan, filters, region of interest, etc.) and possibly also 3-D. The third, or high end, WS will be capable of full 3-D image manipulation and have enough local storage to hold multiple sets of images. The key to this series of workstations is that they would utilize the same biomedical shell (i.e. user interface). Application programs for diagnostic imaging, stereotaxic surgical planning, radiation therapy planning, tumor staging, etc. will also be developed.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10306-01 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Liposome Photolysis

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

P.D. Smith	Physicist	BEIB, DRS
C. Black	Biochemist	ROB, NCI

COOPERATING UNITS *(if any)*

ROB, NCI

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Electronic and Electrical Engineering Section

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.3	0.2	0.1

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The ability to selectively deliver a drug to a specific site is a requirement in many clinical situations. One potential vehicle for this are liposomes which can be made to incorporate the drug. This study examines the prospects of being able to release the drug by lysis following photo-excitation of a dye incorporated into the liposome wall. Several compositions of the liposome preparation have been evaluated each including phthalocyanine which is excited at 670nm.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10307-01 BEI

PERIOD COVERED
October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Pulse Oximeter Calibrator

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

J.M. Schmitt	Staff Fellow	BEIB, DRS
G.X. Zhou	Visiting Scientist	BEIB, DRS
E.C. Walker	Section Chief, ACES	BEIB, DRS

COOPERATING UNITS *(if any)*
None

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Applied Clinical Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.2	0.1	0.1

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Current practice among manufacturers of pulse oximeters is to calibrate an instrument prior to shipment according to a calibration curve based on measurements obtained from a group of human subjects. No means for checking the calibration of pulse oximeters in the clinic now exists. We are designing a device for calibrating pulse oximeters that simulates the optical properties of a pulsating capillary bed containing various fractions of oxygenated and deoxygenated hemoglobin. The design of the calibrator is based on liquid-crystal light modulators which are used to set the dc and modulated (ac) light intensities passing through the "capillary bed." By adjusting the ac/dc intensity ratios in wavelength bands in the red (630-690nm) and infrared (800-1000nm) the display of the oximeter can be set to the desired oxygen saturation (S02) value.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10308-01 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Reflectance-Mode Pulse Oximetry

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

J.M. Schmitt	Staff Fellow	BEIB, DRS
G.X. Zhou	Visiting Scientist	BEIB, DRS
E.C. Walker	Section Chief, ACES	BEIB, DRS
R.T. Wall	Chief, Anesthesia Dept.	ANESTH, CC

COOPERATING UNITS *(if any)*

ANESTH, CC

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Applied Clinical Engineering Section

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.5	0.4	0.1

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Although pulse oximeters have been used extensively over the last few years in clinical monitoring applications, the theoretical basis of pulse oximetry is still poorly understood. As a result, the development of instrumentation has relied on the slow acquisition of empirical knowledge. Recently, clinicians have expressed interest in the possibility of developing a transcutaneous oximeter that operates in the reflection mode, rather than in the transmission mode. Such a device could be used at many sites on the body, and may enable monitoring during shock and other conditions during which peripheral blood flow is compromised. Using a photon-diffusion model, we have studied the effect of tissue blood volume and other important variables on the calibration of reflectance-mode oximeters employing a variety of sensor configurations. Measurements from gelatin/milk tissue phantoms and skin compare favorably with model predictions. We are now constructing prototype solid-state sensors which will be used to measure skin reflectance. New methods for determining blood oxygen saturation from remitted intensities will be tested in hypoxic animal models.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10309-01 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Signal Conditioning and Data Acquisition System for Sleep Deprivation Studies

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

C.P. Mudd	Biomedical Engineer	BEIB, DRS
C.A. Everson	Research Fellow	CPB, NIMH

COOPERATING UNITS *(if any)*

CPB, NIMH

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Applied Clinical Engineering Section

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS: 0.2	PROFESSIONAL: 0.2	OTHER:

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Current studies into sleep disorders involve the simultaneous measurement of a combination of physical parameters. These include EEG, EMG, heart rate, core temperature, and brain temperature. CPB (Clinical Psycho- Biology) is presently investigating sleep disorders using animal models. Rats display similar sleep behavior to humans and are used in this investigation.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10310-01 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Microcalorimeter Measurements of DNA-Protein Interactions

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

C.P. Mudd	Biomedical Engineer	BEIB, DRS
P.D. Ross	Physical Chemist	LMB, NIDDK
V. Tekeda	Research Chemist	FCRF, NCI
R.L. Berger	Research Chemist	LTD, NHLBI

COOPERATING UNITS *(if any)*

LMB, NIDDK; FCRF, NCI; LTD, NHLBI

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Applied Clinical Engineering Section

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.1	0.1	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The use of various proteins to modify the human immune system response is of intense interest in the areas of organ transplants, AIDS, and chemotherapy. At the NCI, several new drugs have been developed for this purpose. At present, these drugs are available only in small amounts (approximately 1 ml). By mixing these drugs with carefully constructed molecules of DNA and measuring the enthalpy, the drug-DNA bond interactions can be determined. Investigators at the NCI and NIDDK consulted BEIB and LTD in regards to measuring the heats of these small samples. We recommended using our tantalum stopped flow microcalorimeter which has the capability of measuring heats of 10 microjoules or less in 80 microliter samples. The first experiments showed that we could measure heats in the range of 5 microjoules with a standard error of less than 0.5 microjoules. Preliminary results show that the enthalpy is very low which indicates that the binding is almost exclusively entropy driven.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10311-01 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Whole Cell Patch Clamp Studies Using High Speed Capitance Measurements

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

A. Markowitz	Electrical Engineer	BEIB, DRS
B. Chidakel	Electronic Technician	BEIB, DRS
T. Tedder	Mechanical Technician	BEIB, DRS
E. Rojas	Biophysicist	LCBG, NIDDK
B. DaCosta	Visiting Scientist	LCBG, NIDDK

COOPERATING UNITS *(if any)*

Laboratory of Molecular Biology, NIDDK

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Applied Clinical Engineering Section

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.6	0.8	0.8

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Whole cell patch clamp technology provides a means for measuring membrane capacitance of cell channels. Applications included measuring membrane capacity due to the action of synexin on medullary chromaffin cells. Programmed pipette potential changes were obtained from a D/A converter of a PACE minicomputer system. Current transients were obtained and read into the high speed (500 kHz) A/D converter of this system.

A moderate speed (150 kHz) PC-based microcomputer system is currently being developed for membrane capacitance measurements.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10312-01 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT (80 characters or less. Title must fit on one line between the borders.)

Computer Connectivity of HPLC Systems in the Analysis of Ascorbic Acid Enhancement on Chromaffin Cells

PRINCIPAL INVESTIGATOR (List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)

A. Markowitz	Electrical Engineer	BEIB, DRS
M. Levine	Senior Investigator	LCBG, NIDDK

COOPERATING UNITS (if any)

Laboratory of Molecular Biology, NIDDK

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Applied Clinical Engineering Section

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.6	0.4	0.2

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK (Use standard unreduced type. Do not exceed the space provided.)

A local area network connecting real time laboratory experiments is required by many laboratories. As one computer is running an experiment, the network can have another computer process the data as well as performing data collection backup for all computer controlled experiments.

Multiple setups for the detection of ascorbic acid in bovine chromaffin cells using high-performance liquid chromatography with coulometric electrochemical detection were networked in the laboratory. The system consisted of two PS2 Model 80 microcomputers and two NEC Powermate 2 APCIV microcomputers with Maxima 820 and Baseline 810 HPLC hardware and software. The network will transfer laboratory data between machines and perform other network functions. The automated data collection hardware and software were modified to enable it to work in a network environment. The system design was developed and implemented in a ring topology using a token ring network and a IBM PC LAN operating system.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10313-01 BEI

PERIOD COVERED
October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
High Speed Multi-Channel Spectrophotometer

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

W.S. Friauf	Chief, EEES	BEIB, DRS
P.D. Smith	Physicist	BEIB, DRS
R.W. Hendler	Section Chief	LC, NHLBI
J. Cole	Electrical Engineer	BEIB, DRS
H. Frederickson	Programmer	CSL, DCRT

COOPERATING UNITS *(if any)*

Laboratory of Cell Biology, NHLBI; CSL/DCRT

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electrical and Electronic Engineering

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.3	0.3	

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A number of commercial multichannel spectrophotometers using charge-coupled devices have been developed recently for general use in biomedical research. We have explored the possibility of improving both the speed and accuracy of such instruments by exploiting other new devices.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10314-01 BEI

PERIOD COVERED
October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Pulsed Photo-Dynamic Therapy

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

W.S. Friauf	Chief, EEES	BEIB, DRS
J. Cole	Electrical Engineer	BEIB, DRS
A. Russo	Section Chief	ROB, NCI

COOPERATING UNITS *(if any)*
Radiation Oncology Branch, NCI

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electrical and Electronic Engineering

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.2	0.2	

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Experimental evidence indicates that the efficacy of photodynamic therapy (PDT) is temperature dependent. This opens the possibility of using a temperature gradient in the tissue to partially compensate for the rapid attenuation of light, thus allowing effective treatment to a greater depth. By pulsing the surface temperature at an appropriate rate and illuminating only during the cool phase, the treatment at a selected depth will occur during the warm phase due to the propagation delay experienced by the temperature wave.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10315-01 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

A Model of Magnetic Stimulation of a Nerve Fiber

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

B.J. Roth	Staff Fellow	BEIB, DRS
P. Basser	Staff Fellow	BEIB, DRS
L.G. Cohen	Visiting Associate	MNB, NINDS
M. Hallett	Clinical Director	MNB, NINDS

COOPERATING UNITS *(if any)*

Medical Neurology Branch, NINDS

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Mechanical Engineering

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.5	0.5	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A model is presented to explain the physics of nerve stimulation by electromagnetic induction. Maxwell's equations predict the induced electric field distribution that is produced when a capacitor is discharged through a stimulating coil. A non-linear cable model, containing active Hodgkin-Huxley elements, describes the response of the nerve fiber to this induced electric field. It is shown that the nerve fiber is stimulated by the gradient of the component of the induced electric field that is parallel to the fiber, which hyperpolarizes or depolarizes the membrane and may stimulate an action potential. Once the coil's position, orientation and shape are given and the resistance, capacitance and initial voltage of the stimulating coil are specified, this model predicts the resulting transmembrane potential of the fiber as a function of distance and time. Finally, it predicts complicated dynamics such as action potential annihilation and dispersion.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10316-01 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Calculation of Electric Fields During Magnetic Stimulation

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

B.J. Roth	Staff Fellow	BEIB, DRS
W.S. Friauf	Section Chief	BEIB, DRS
J. Saypol	Guest Researcher	BEIB, DRS
L.G. Cohen	Visiting Associate	MNB, NINDS
M. Hallett	Clinical Director	MNB, NINDS

COOPERATING UNITS *(if any)*

Medical Neurology Branch, NINDS

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Mechanical Engineering

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS: 0.6	PROFESSIONAL: 0.6	OTHER:

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Magnetic stimulation is a new technique for activating neurons that is both painless and noninvasive. Stimulation occurs when a brief current pulse is passed through a coil placed near the neuron, producing an electric field by electromagnetic induction. The goal of this project is to develop mathematical models to calculate the electric field induced in the human body during magnetic stimulation. Two models are developed in detail: 1) a model of the stimulation of a peripheral nerve in the arm, and 2) a model of the stimulation of the brain.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10317-01 BEI

PERIOD COVERED
October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
New Algorithms for the Processing of Biomedical Images

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

Michael Unser	Visiting Associate	BEIB, DRS
Akram Aldroubi	Staff Fellow	BEIB, DRS
Murray Eden	Chief	BEIB, DRS

COOPERATING UNITS *(if any)*
None

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Office of the Chief

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0	0	

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Textural information can play an important role in interpretation of a variety of biomedical images, such as X-rays and ultrasound recordings. We have developed a texture segmentation method using texture features extracted by linear filtering. An important component of this system is a new multi-resolution feature reduction module which offers a substantial performance improvement over conventional approaches (principal components or Karhunen-Loève transform).

It is often desirable to reduce the measurement noise that is present in a variety of biomedical images, such as high resolution micrographs, echocardiograms or PET scans. Conventional linear filtering techniques perform well for homogeneous regions but tend to degrade sharp image transitions. In order to preserve the edge information, we have designed an adaptive least squares post-filtering procedure which locally computes a linear combination between the initial noisy image and its filtered version to minimize the estimation error. This method is computationally very efficient and allows an a posterio compensation of some of the deficiencies of conventional noise reduction techniques.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10318-01 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Apple Macintosh II Based Image Processing Workstation

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

Michael Unser Visiting Associate BEIB, DRS

COOPERATING UNITS *(if any)*

None

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Office of the Chief

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0	0	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Until very recently, the integration of image processing systems required considerable expense for the acquisition of specialized hardware, in addition to a major programming effort. As a consequence, image processing has been accessible only to a minority of privileged researchers. With the recent advent of powerful personal computers such as the Macintosh II, this situation is bound to change dramatically. Although such computers offer low-cost hardware configurations for simple image processing tasks, their programming using conventional techniques is notoriously difficult, due to the high level of sophistication of the user interface.

The main purpose of this project was to devise powerful development tools to facilitate the development of specialized image processing software for such workstations. The first step was to create a simple image processing shell which is extremely easy to modify for creating specialized applications; the main feature is that all complex interactions with the user interface are handled automatically and that the programmer need only be concerned with the application-specific procedures. The second aspect was to develop a comprehensive set of basic image processing modules. At present, our software library includes about 200 FORTRAN subroutines that perform image processing tasks such as filtering, edge detection, point transformations, and binary operations.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10319-01 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Calculation of Electrical Activity in Thick Strands of Cardiac Tissue

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and Institute affiliation)*

B.J. Roth	Staff Fellow, MES	BEIB, DRS

COOPERATING UNITS *(if any)*

None

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Mechanical Engineering

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.1	0.1	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A numerical simulation has been performed of the propagation of an action potential through a thick cylindrical strand of cardiac tissue. The bidomain model was used to account for the effect of tissue anisotropy and the interstitial space on current flow, and the Beeler-Reuter model was used for the electrically active membrane properties. A relaxation technique was used to solve the nonlinear partial differential equations. The simulation predicts: 1) the shape of the wavefront across the strand cross-section, 2) the dependence of the conduction velocity on the strand radius and on the radii of the individual cells, 3) the length constant of the tissue, as measured by subthreshold cable analysis, and how it is affected by tissue anisotropy, and 4) the effect of tissue edema (changes in the volume fraction of the extracellular space) on propagation.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10320-01 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Computerized Methods for Analyzing Two-Dimensional Agarose Gel Electrophoretograms

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

A. Aldroubi	Staff Fellow	BEIB, DRS
M. Unser	Visiting Associate	BEIB, DRS
D. Tietz	Visiting Scientist	LTPB, NICHHD
B. Trus	Research Chemist	CSL, DCRT
A. Chrambach	Senior Staff	LTPB, NICHHD

COOPERATING UNITS *(if any)*

NICHHD, DCRT

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Office of the Chief

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
	0	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Previous methods to interpret zonal or polydisperse gel patterns of two-dimensional Serwer-type gels for the size and free mobility (surface net charge density) of each component could not simultaneously measure the abundance of the components. Our work advances the method by specifying the relative concentration of each component on the basis of the densitometric analysis of the pattern. We have established suitable procedures and their underlying algorithms. We have implemented the mathematical routines in a user-friendly software package for use on a personal computer.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10321-01 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Nuclear Magnetic Resonance Instrumentation Group

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

D. Hoult BEIB, DRS

COOPERATING UNITS *(if any)*

None

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Nuclear Magnetic Resonance

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0	0	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

BEIB continues to explore and support the numerous research opportunities presented by the *in vivo* application of nuclear magnetic resonance. Work has focused on three main areas: the design and construction of specialized radio frequency coils, the development of new spin "massaging" techniques and the implementation of echo-planar imaging--a method which aims to produce images in under 100ms. With the realization that NMR may be used to monitor temperature non-invasively (via measurement of water's diffusion constant), a considerable effort has been made to produce dual probes that not only give the NMR signal, but which produce an intense r.f. electric field that generates localized hyperthermia in cancer patients. Accurate monitoring of temperature has been the biggest barrier to the safe implementation of the hyperthermia technique. Coils have also been made for localized spectroscopy on animals and for echo-planar head imaging at 64 MHz. New spin techniques have been implemented. These include: selective noise pulses (devised with the aid of the VAX computer system that the group continues to support), which effectively "scramble" magnetization over a well-defined region and thereby suppress signal; modification of the well-known STEAM and PRESS sequences to obtain proton spectra from 0.5 ml volumes in cat heads; new echo-planar imaging sequences which monitor diffusion and which use asymmetric gradient switching to obtain resolution of under 0.5mm. A large construction project has resulted in the fabrication of a shielded gradient coil system for a two tesla magnet, and the coils are new ready for testing. At the same time, powerful local z-gradient coils, for use with echo-planar and diffusion measurements, have been built and successfully tested. Finally, the writing of a book "Biomedical Magnetic Resonance Technology" has been completed, publication being expected in November, 1989; a sensitive way of monitoring residual Bo gradients following gradient switching has been invented; a novel energy transfer system for rapid gradient switching has been devised (patent applied for), and the *in vivo* Center's computing system has been further refined and improved.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10322-01 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Construction of a Data Acquisition System for an Ultrahigh Resolution Dedicated Scanning Transmission Electron Microscope

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

C.R. Swyt	Physical Scientist	BEIB, DRS
C.E. Fiori	Physical Scientist	BEIB, DRS

COOPERATING UNITS *(if any)*

None

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Electron Beam Imaging and Microspectroscopy Group, Office of the Chief

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
2.0	2.0	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

An automated data acquisition system for the Vacuum Generators HB 501 ultrahigh-resolution dedicated scanning transmission electron microscope is being developed. The new analytical capabilities of this class of electron microscope require fresh approaches to computerization of data acquisition and analysis and it is for this reason that we were required to construct our own system rather than assemble commercial products. The completed and nearly completed components of the data acquisition system obtain x-ray spectra from the microscope and perform a wide range of mathematical and physical procedures to extract chemical information concerning the specimen under observation. The system is comprised of a Macintosh II computer with several National Instruments interface plug-in bus cards and an extensive computer program that uses Macintosh and National Instrument routines to control the Macintosh-user interface and the cards. Components of the acquisition system are under active development, but some months away from completion are the bright and dark field imaging and the electron energy loss modes.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10323-01 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Sulfone Structure-Activity Analysis

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

P.F. Morrison	Physical Scientist	BEIB, DRS
C.J. Allegra	Physician	MB, NCI

COOPERATING UNITS *(if any)*

Medicine Branch, NCI

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Chemical Engineering Section

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.2	0.2	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Structure-activity analysis has been employed to identify new sulfone compounds that exhibit strong activity against Toxoplasma gondii, a protozoan capable of inducing serious infection in AIDS patients. Since it has been observed that most of these patients can tolerate the only commercially available sulfone, dapsone, alternative agents were sought within this class of compounds. Several sulfone analogs, including dapsone, were identified as potent inhibitors with IC50s<1μM. However, none of the analogs was more active in the mean than dapsone itself. Accordingly a Fujita-Ban formalism was used to determine the contributions of each analog substituent to drug potency and to assess whether new combinations of these substituents could lead to improved analogs. Of 21 moieties investigated, 2'-NH$_2$, 2'-SO$_2$NH$_2$, 4'-NH(CH2)$_2$OH, and 3'-Cl substitutions on dapsone were found to be most likely to potentiate activity against T. gondii. Further inhibition studies against the purified enzyme target ruled out a significant potentiating capability of the aminoethanol derivative. However, testing of the 3'-Cl derivative against intact organisms revealed a five-fold increase in activity over that obtained with dapsone. These studies suggest that the sulfones may be important therapeutic agents for the treatment of T.gondii infections.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10324-01 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

In Vitro Hemodynamic Models for Cardiovascular Studies

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

R.J. Lutz	BEIB, DRS
J. Peacock	NHLBI, IR, CB
M. Leon	NHLBI, IR, CB
A. Bartalluci	NHLBI, IR, CB
M. Chulay	CC, NURS
L. Rosa	NINCDS, IR, SN
J. Doppman	CC, DR
J. Cannon	Howard Univ.

COOPERATING UNITS *(if any)*

NHLBI, NINCDS, CC, Howard University

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Chemical Engineering Section

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
3.0	2.0	1.0

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Physical models of vascular systems are being used extensively in our laboratory to study a variety of hemodynamic phenomena. The projects during the past year are in five major categories: (1) a study of flow in coronary arteries and the influence of arterial stents on the development of turbulence; (2) the application of diastolically-phased, high velocity pulsed injections to reduce streaming during intracarotid administration of BCNU solutions for treating brain tumors; (3) a study comparing effects on vascular patency and hemolysis of blood withdrawal by vacutainers, versus a manual syringe method; (4) a study of flow around a sphere concentric to a tube as an idealized model of a balloon catheter in a vessel; and (5) an investigation of the streaming of pancreatic gastrin secretions due to the stable flow field at the confluence of the superior mesenteric and splenic veins into the portal vein.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10325-01 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Noninvasive Magnetic Measurement of Current in Peripheral Nerve

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

B. Roth	Staff Fellow	BEIB, DRS
S. Sato	Neurologist	MNB, NINDS

COOPERATING UNITS *(if any)*

Medical Neurology Branch, NINDS

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Mechanical Engineering

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS: 0.25	PROFESSIONAL: 0.25	OTHER:

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The magnetic field and electric potential produced by action currents in a human median nerve have been measured in normal volunteers. A mathematical model has been developed relating the measured magnetic field to the current distribution. The project is aimed at developing a noninvasive technique to monitor peripheral nerve regeneration in patients who have suffered localized nerve damage.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10326-01 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Analytical Electron Microscopy of Pancreatic Islet of Langerhans

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

R.D. Leapman	Physical Scientist	BEIB, DRS
M. Foster	Physicist	BEIB, DRS
M.X. Li	Visiting Scientist	LCBG, NIDDK
I. Atwater	Biophysicist	LCBG, NIDDK

COOPERATING UNITS *(if any)*

LCBG, NIDDK

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Electron Beam Imaging and Microspectroscopy Group

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.2	1.2	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The compositions of individual secretory granules have been measured using electron probe x-ray microanalysis in resting, or unstimulated, pancreatic islet cells. Islets were isolated by collagenase digestion from adult rats, incubated for 2 to 3 hours in culture medium at 37° C in the presence of 5.6 mmol/l glucose, frozen, and cryosectioned. Cryosections were freeze-dried and analyzed in the electron microscope. Granules in some cells contained high levels of sulfur and zinc, attributable to insulin storage organelles in beta cells. Granules in other cells contained low levels of sulfur and no detectable zinc, attributable to glucagon-containing secretory organelles in alpha cells. Phosphorus content was high in granules of both alpha and beta cells, consistent with other observations that ATP is concentrated in secretory granules. Granule calcium concentrations typically varied from 10 to 80 mmol/kg dry weight within a beta cell. Zinc content of beta granules was approximately 30 mmol/kg dry weight and sulfur content approximately 400 mmol/kg dry weight, quantitatively consistent with other data on the zinc-insulin storage complex. Interestingly, a few granules with composition characteristic of beta granules were found in non-beta cells.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10327-01 BEI

PERIOD COVERED
October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Mass Mapping in the High Resolution Scanning Transmission Electron Microscope

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

R.D. Leapman	Physical Scientist	BEIB, DRS
A.C. Steven	Visiting Scientist	LPB, NIAMS
F. Booy	Visiting Scientist	LPB, NIAMS
S.B. Andrews	Chemist	LN, NINCDS
J. Hunt	Electronics Engineer	Lehigh Univ.
C.E. Fiori	Physical Scientist	BEIB, DRS

COOPERATING UNITS *(if any)*
LPB, NIAMS; LN, NINCDS; Lehigh University

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electron Beam Imaging and Microspectroscopy Group

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.3	.3	

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Digitized dark-field scanning transmission electron microscope images were acquired using a PC-AT computer system. The computer was interfaced to the Vacuum Generators HB501 STEM and used to generate a rapid scan of the nanometer size electron probe (approximately 50 microseconds per pixel). The annular dark-field signal was measured by counting single elastically scattered electrons at each pixel. Images were analyzed on a Macintosh II computer, allowing quantitative measurements of masses of macromolecules to be made. Initial tests were performed on freeze-dried T4 bacteriophages.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10328-01 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Measurement of Free Calcium in Single Frog Oocytes

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

A. Eidsath	Staff Fellow, MES	BEIB, DRS
K. Catt	Chief, ERRB	NICHHD

COOPERATING UNITS *(if any)*

Endocrinology and Reproduction Research Branch

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Mechanical Engineering

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.2	0.2	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Certain external stimuli cause an increase in the free calcium level in the cytoplasm of a frog oocyte. The standard way to measure this is using the biological photoprotein aequorin, which reacts with calcium to emit light. The goal of the project is to be able to measure the relative amounts of calcium produced by various stimulating agents by measuring the number of photons emitted after the stimulus. The emitted light is at an extremely low level--about 50 photons per second--so a very low dark current photomultiplier tube and a cooled housing were used. The oocyte is inserted into a specially-designed stopped-flow cell so the external stimuli can be changed very quickly. Special optics were used to capture as much light as possible and focus it on the photomultiplier tube.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10329-01 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Optimized Mammography Instrument

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

A. Eidsath	Staff Fellow, MES	BEIB, DRS
S. Leighton	Mechanical Engineer	BEIB, DRS
J. Vucich	Clinical Radiology	NIH
R. Jennings	Research Scientist	FDA

COOPERATING UNITS *(if any)*

National Center for Devices and Radiological Health, FDA

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Mechanical Engineering

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.5	0.5	

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Mammography plays a vital part in the early detection of breast cancer. Unfortunately, mammography units being used today have never been analyzed from a systems point of view. Multiparameter optimization studies of a mammography system have been reported by Muntz et al (Med. Phys **12**, 5, 1985) in which the patient dose has been minimized, while maintaining satisfactory image quality. The most important new feature of the design is the presence of an array of thin metal vanes arranged in an arc about the x-ray source, between the breast and the film. The vanes absorb scattered radiation and thus improve the quality of the image. In order for the vanes not to image on the film the grid must move in a precisely controlled profile during the exposure.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10330-01 BEI

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Kinetics of Erythrocyte Sickling in Physiological Conditions

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

A. Eidsath	Staff Fellow, MES	BEIB, DRS
W. Eaton	Acting Chief. LCP	LCP, NIDDKD
J. Hofrichter	Senior Staff	LCP, NIDDKD

COOPERATING UNITS *(if any)*

Laboratory of Chemical Physics, NIDDKD

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Mechanical Engineering

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.3	0.3	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

We are using a flow cell in which the partial pressure of oxygen can be varied rapidly in order to study sickling under conditions that more resemble physiological conditions than have been used in the past. Since there is a broad distribution in the cellular hemoglobin concentration, many cells need to be analyzed simultaneously. The change in shape of the cells in the flow cell is observed under a microscope. A video camera transmits the picture to a computer, where the fraction of cells that have sickled can be automatically determined using image analysis algorithms.

VETERINARY RESOURCES BRANCH
DIVISION OF RESEARCH SERVICES
NATIONAL INSTITUTES OF HEALTH

FY 1989 VRB ANNUAL REPORT

Dr. Stephen Potkay, Chief

VETERINARY RESOURCES BRANCH
DIVISION OF RESEARCH SERVICES
NATIONAL INSTITUTES OF HEALTH

FY 1989 VRB ANNUAL REPORT

Dr. Stephen Potkay, Chief

VRB Research Project (Z01 RS)

No.	Title	Investigator	Page No
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00073-05	Lipid Metabolism of the *Macaca fascicularis*	D. Barnard	8
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DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 00001-19 VR

PERIOD COVERED
October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Animal Model Development

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI: Carl T. Hansen Geneticist SAS, VRB, DRS

COOPERATING UNITS *(if any)*

LAB/BRANCH
Veterinary Resources Branch

SECTION
Small Animal Section

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.0	1.0	0

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The objective of this program is developing new models for biomedical research utilizing the natural genetic variation found in sexually reproducing small research animals. The emphasis has been with certain mutants which are known to affect the functioning of the immune system, metabolic and neurological systems in rats and mice. The strategy has been to establish these mutants on different genetic backrounds as well as making different combinations of independantly appearing mutants. The result has been the formation of a unique resource of animal models which is gradually finding increasing acceptance by the research community.

PHS 6040 (Rev. 1/84)

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 00051-09 VR

PERIOD COVERED

October 1, 1988 through September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Reproduction in Mutant Sheep used for the Study of Hyperbilirubinemia

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	L.D. Stuart	Chief	UU, ACS, VRB, DRS
Others:	D.E. Wildt	Reproductive Physiologist	NZP, Smithsonian Institution
	S.C. Kalser	Director	Liver Diseases Prog, DDN, NIAID
	P.K. Chakraborty	Head	Research Division, Dept. of OB-GYN, USUHS

COOPERATING UNITS *(if any)*

Digestive Diseases and Nutrition Program, National Institutes of Arthritis, Metabolism and Digestive Diseases

LAB/BRANCH

Veterinary Resources Branch

SECTION

Animal Center Section

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.2	.1	.1

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A specific genetic strain of Corriedale sheep is used as an animal model for the study of liver pathophysiology, specifically, hyperbilirubinemia (Dubin-Johnson Syndrome). This project is concerned with increasing the numbers of animals available for research by the controlled breeding of individuals which genetically transmit this character. This project is utilizing what is considered to be the only existing Corriedale sheep homozygotic for this trait. Efforts are being made to obtain both homozygous and heterozygous offspring from these highly inbred individuals. Semen collected artifically from the homozygotic rams was diluted in various cryoprotective extenders and then freeze preserved. This will ensure the long term availablity of male gametes for artifical insemination. Overall this project allows prepetuation of this specific gene pool and ensures availability of research animal for future investigations of Dubin-Johnson Syndrome and related metabolic disorders.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS-00071-05 VR

PERIOD COVERED
October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Development of Genetic Profiles for Inbred Laboratory Rodents

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

J.S. Crowell, Geneticist	Comparative Pathology Section, VRB, DRS
S.L. Finley, Biochemist	Comparative Pathology Section, VRB, DRS

COOPERATING UNITS *(if any)*
Small Animal Section, VRB, DRS

LAB/BRANCH
Veterinary Resources Branch

SECTION
Comparative Pathology Section

INSTITUTE AND LOCATION
Division of Research Services, Bethesda, Maryland 20892

TOTAL MAN-YEARS	PROFESSIONAL:	OTHER
0.5	0.4	0.1

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project is designed to identify and locate on the chromosomes of inbred rodents inherited characteristics which can be used in a wide range of biomedical research and to further the ability of the Genetic Monitoring Unit to perform its basic mission. The major areas of interest are: 1) characterization of the genetic traits by biochemical and immunological techniques; 2) chromosome mapping by standard genetic analysis; and 3) application of the genetic characteristics to explore new animal models of pathogenesis.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 00073-05 VR

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Lipid Metabolism of the Macaca fascicularis

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	Dennis Barnard	Biologist	SAS, VRB, DRS
	Joseph Knapka	Physiologist	SAS, VRB, DRS

COOPERATING UNITS *(if any)*

LAB/BRANCH

Veterinary Resources Branch

SECTION

Small Animal Section

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.6	0.1	0.5

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The study will examine the metabolism of exogenous fatty acids by Macaca fascicularis. Trans fatty acids which cannot be synthesized by eukaryotes will be used as the exogenous fatty acid marker. These fatty acids are geometrical isomers of cis fatty acids which can be synthesized by eukaryotes. The trans fatty acids are catabolized and removed from the body shortly after the fatty acids are removed from the diet. Twelve male M. fascicularis monkey were used in the study. Six were fed the control diet, and the others received the experimental diet. The RBC membrane of monkeys fed the control diet contained .5% trans octadecanoate isomers of the fatty acids. Examination of the fecal fatty acids from these monkeys showed that biohydrogenation does occur in their gut producing trans fatty acids which appear to be incorporated into the RBC membrane. Within 6 weeks after initiating the study the RBC membranes of monkeys fed the experimental diet contained 10.8% trans octadecanoate isomers of the total fatty acids. DPH steady state fluorescence polarization analysis of the erythrocyte membrane fluidity showed no change in membrane fluidity between the monkeys fed the two diets. However, insulin binding activity was altered in the monkeys fed the diet containing trans fatty acids.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 00077-05 VR

PERIOD COVERED
October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Development of an Embryo Cryopreservation Program in Laboratory Animals

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	Patricia M. Schmidt	Physiologist	SAS,VRB,DRS
	Carl T. Hansen	Geneticist	SAS,VRB,DRS
	David E. Wildt	Guest Researcher	VRB,DRS
	William F. Rall	Guest Researcher	VRB,DRS

COOPERATING UNITS *(if any)*

LAB/BRANCH
Veterinary Resources Branch

SECTION
Small Animal Section

INSTITUTE AND LOCATION
DRS,NIH,Behesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
3.0	2.0	1.0

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The program objective is to facilitate the management of the NIH Animal Genetic Resource (NIHAGR) through the development and utilization of techniques such as collection, culture, freezing and transfer of embryos and gametes for cryobanking genetic material and improving reproductive potential. The NIHAGR maintains a number of critical species and, within species, a vast number of invaluable genotypes used in biomedical research. Embryo preservation uses a cryoprotectant in the freezing medium which allows sufficient dehydration to protect the blastomeres during freezing. Following thawing and dilution of the cryoprotectant, embryos are cultured to assess _in vitro_ development. Transplantation of embryos into recipient females monitors _in vitro_ fertilization and ova freezing are being examined as techniques to salvage limited genetic material from single females or strains with poor _in vitro_ fertilization rates. Banked embryos are maintained in a frozen state until needed for rederivation. A primary focus of laboratory efforts is the study and optimization of cryobanking technology in mice and rabbits and more recently, in rats. A major research finding is that embryo freezability is confounded and influenced markedly by mouse genotype. Such responses have been examined in over 56 genotypes, most of which display genotype-specific survival rates to standardize embryo freeze-thawing procedures. Ancillary projects are oriented toward the comparative aspects of improving long-term embryo storage with particular emphasis on the study of cryoprotectants and enhancing methods for embryo freezing, thawing, dilution and transfer. Efforts in the rabbit focus on improvements in collection procedures and preservation of embryos.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 00078-04 VR

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Serum Cholesterol Values of the NIH WHHL Rabbit

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	Dennis Barnard	Biologist	SAS, VRB, DRS
	Cheri Reid-Quinn	Veterinarian	SAS, VRB, DRS
	William Watson	Veterinarian	SAS, VRB, DRS
	Joseph Knapka	Physiologist	SAS, VRB, DRS

COOPERATING UNITS *(if any)*

LAB/BRANCH

Veterinary Resources Branch

SECTION

Small Animal Section

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.0	0.5	0.5

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The Veterinary Resources Branch, Division of Research Services established a Watanbe Hyperlipidemic Rabbit (WHHL) breeding colony to be used as a resource for investigators requiring the use of this animal model. The colony is being characterized for serum triglyceride levels. Blood is being collected from rabbits at the following ages: six weeks, three months, seven months, and one year. Total serum cholesterol values ranged from 310 to 1251 mg/dl with a mean of 828 mg/dl. The low density lipoprotein (LDL) cholesterol values ranges from 1185 mg/dl with a mean of 630 mg/dl. Thus 80% of the total cholesterol was composed of LDL cholesterol. There was a substantial decrease from 885 to 576 mg/dl in serum total cholesterol between the ages of eight weeks and one year. The most significant decrease occurred between the ages of 15 to 25 weeks. There was no difference in total cholesterol concentrations due to sex. The serum triglyceride values ranged from 107 to 959 mg/dl with a mean of 394 mg/dl within one year of age. The serum triglyceride concentration decreased to 349 mg/dl within one year of age. The serum triglyceride concentration was influenced by the sex of the rabbit. The mean male and female serum triglyceride concentrations were 510 mg/dl and 309 mg/dl respectively.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 00080-03 VR

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Effects of Progesterone on CEH in the SLA Inbred Miniature Pig

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	K.J. Lipetz	Director of Lab.	Montgomery Infertility Inst.
Others:	L.D. Stuart	Chief	UU, ACS, VRB, DRS
	N.L. Garnett	Vet. Med. Officer	ARP, DRR

COOPERATING UNITS *(if any)*

LAB/BRANCH

Veterinary Recources Branch

SECTION

Animal Center Section

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.05	.025	.025

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The SLA inbred miniature pig herd, bred and maintained by the Ungulate Unit for the Immunology Branch, NCI typically produces a small litter and exhibits a variety of reproductive problems not found in the standard-sized pig. A uterine condition, cystic endometrial hyperplasia (CEH), exists in the herd. Sows that are not bred until after one year of age have a high incidence of CEH and are incapable of reproduction. Regression or reduction of the incidence of CEH would improve greatly the reproductive performance of the herd. Previous studies have shown the SLA inbred miniature pig has a serum progesterone level considerably lower than the standard-sized pig. The effects of long term administration of progesterone of CEH will be studied.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 00081-03 VR

PERIOD COVERED

October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Control of Luteal Function and Induction of Ovulation and Conception in the Anestrus Bitch.

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI.	P. K. Chakroborty	Head, Research Division Obstetrics & Gynecology	USUHS
Others:	R. L. Killens	Chief, Carnivore Unit	ACS/VRB/DRS
	J. L. Brown	Research Associate Obstetrics & Gynecology	USUHS

COOPERATING UNITS *(if any)*

Carnivore Unit, ACS, VRB, DRS; Research Division, Department of Obstetrics and Gynecology, USUHS.

LAB/BRANCH

Veterinary Research Branch

SECTION

Animal Center Section

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.6	.4	.2

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project is designed to study the effect of two treatment regimens using hormone stimulants to induce ovulation and conception in bitches. The major areas of interest are: 1) the induction of regression of the functional corpora lutea by hormone administrative; and 2) the induction of follicular development and ovulation followed by breeding bitches pretreated with hormone to regress corpora lutea.

DEPARTMENT OF HEALTH AND HUMAN SERVICES · PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 00082-02 VR

PERIOD COVERED

October 1, 1989 through September 30, 1990

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Acute Effects of Thromboxane Synthetase Inhibition in Gravid Macaques

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	D. Jarrell	Chief	PU, ACS, VRB, DRS
Others:	F. Judge	Acting Chief	ACS, VRB, DRS
	J. Keith	Assoc. Prof.	VMRCVM (VA-MD Reg. Col. Vet. Med.)

COOPERATING UNITS *(if any)*

VA-MD Regional College of Veterinary Medicine

LAB/BRANCH

Veterinary Resources Branch

SECTION

Animal Center Section

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.050	0.025	0.020

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Preeclampsia is a hypertensive disease of late pregnancy and is a major cause of maternal and fetal mortality and morbidity. Five to ten percent of all pregnancies and up to 20 percent of primagravidas are affected yearly in the United States. The only curative treatment for this syndrome is early delivery, resulting in many neonatal complications due to prematurity.

Recently several laboratories have documented low levels of prostacyclin (PG12) and/or elevated levels of thromboxane A2(TxA2) 1-5. Similar results have been seen in this disease in an ovine model of preeclampsia, and beneficial, effects of thromboxane synthetase inhibitors have been reported in the ovine model. However, the effects of thromboxine synthetase inhibitors have not been studied in gravid primates.

The purpose of this study is to determine the effects of CGS 12970, 3-methyl-2 (3-pyrodyl)-1-idoleoctanoic acid, a thromboxane synthetase inhibitor, in gravid nonhuman primates (rhesus).

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 00083-02 VR

PERIOD COVERED
October 1,1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Mouse Strain Susceptibility to Bacillus piliformis.

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	K.S. Waggie	Chief, Microbiology Unit	CPS,VRB,DRS
	C.T.Hansen	Geneticist	SAS,VRB,DRS

COOPERATING UNITS *(if any)*

LAB/BRANCH
Veterinary Resources Branch

SECTION
Comparative Pathology Section and Small Animal Section

INSTITUTE AND LOCATION
DRS,NIH Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.06	.02	04

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The objective of this project was to find a mouse strain that is susceptible to B. piliformis infection via the oral (natural) route. A susceptible strain would aid in pathogenesis studies and might act as sentinel animals to detect naturally occurring infections in rodent colonies.

Mice with various immunodeficiencies were orally inoculated with B. piliformis spores. Mice were killed 5 days post-inoculation and examined for gross lesions. Tissues were also collected for histopathology. Mouse strains utilized were as follows: CBA/N, P/N, C3H/HeJ, C3H/HeN (C3H), C3H-nu, C3H-bg, C3H-xid, C3H-bg,nu; C3H-bg,xid; C3H-nu,xid.

No significant gross lesions were present in any of the inoculated mice. Cecocolitis was microscopically evident in C3H-bg,nu mice, however, no B. piliformis -like bacteria were observed in silver stained sections. Further studies need to be done to determine if C3H-bg,nu mice are susceptible to B. piliformis infection and, if so, if they would be a suitable sentinel animal.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 00084-02 VR

PERIOD COVERED
October 1, 1988 to September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Development of Genetic Profiles for Inbred Laboratory Rodents

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

J.S. Crowell, Geneticist	Comparative Pathology Section, VRB, DRS
S.L. Finley, Biochemist	Comparative Pathology Section, VRB, DRS

COOPERATING UNITS *(if any)*

Small Animal Section, VRB, DRS

LAB/BRANCH
Veterinary Resources Branch

SECTION
Comparative Pathology Section

INSTITUTE AND LOCATION
Division of Research Services, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.5	0.4	0.1

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project is designed to identify and locate on the chromosomes of inbred rodents inherited characteristics which can be used in a wide range of biomedical research and to further the ability of the Genetic Monitoring Unit to perform its basic mission. The major areas of interest are: 1) characterization of the genetic traits by biochemical and immunological techniques; 2) chromosome mapping by standard genetic analysis; and 3) application of the genetic characteristics to explore new animal models of pathogenesis.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 00085-01 VR

PERIOD COVERED

October 1, 1988 through September 30, 1989

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Modification of the Breeding Cycle of Sheep by Melatonin

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	L.D. Stuart	Chief	UU, ACS, VRB, DRS
Others:	D.M. Jarrell	Chief	PU, ACS, VRB, DRS
	L. Tamarkin	Assistant Prof.	University of Maryland
	M.A.A. Namboodiri	Assistant Prof.	Georgetown University
	J.E. Pierce	Guest Researcher	NHLBI, NIH

COOPERATING UNITS *(if any)*

LAB/BRANCH

Veterinary Resources Branch

SECTION

Animal Center Section

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Maryland 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.6	.1	.5

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project is designed to control the breeding cycle in sheep and to breed ewes out of season. Data exists that indicated the rhythmic secretion of the pineal hormone, melatonin, regulates seasonal breeding in a variety of mammals, including sheep. Sheep usually breed in the fall when elevated levels of ciruclation melatonin are longer (mimicking the longer night). During the spring when levels of melatonin are shorted, sheep enter a period of anestrus. Elevated levels of melatonin will be maintained by daily feeding of melatonin.

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